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LOCAL INJECTIONS AND REGIONAL ANALGESIA WITH PROCAINE SOLUTIONS FOR INTRACTABLE PAIN IN CHRONIC ARTHRITIS AND RELATED CONDITIONS *

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INTRODUCTION

ARTHRITIS and related diseases present systemic and local symptoms not infrequently dominated chiefly by persistent, intractable pain or discomfort. Certain of these rheumatic conditions are preëminently painful, such as neuritis, bursitis, fibrositis and traumatic conditions of muscle, tendon, fascia and joint. While rheumatoid arthritis often is associated with discomfort, it is not as likely to present localized, intractable involvement of one or more joints, as osteoarthritis. We have been impressed by the frequency of severe, localized pain in many of these ailments, for which ordinary systemic and local measures fail to give sufficient or enduring relief.

In rheumatic disease especially, the tendency towards chronicity is aggravated by the accompanying pain. A vicious cycle of pain, muscle spasm, postural defect, disability and deformity often arises. A good part of this picture is functional and depends largely upon the underlying painful state. The appearance of advanced arthritis and related disease frequently suggests that this secondary functional cycle, although starting as a by-product of the disease, becomes responsible for many of the terminal organic changes and trophic disturbances. Because of the dynamic rôle played by localized pain in these conditions, we have sought some means of more satisfactory control of articular and allied discomfort until the usual measures achieve their more gradual effects.

The effort to relieve the arthritic by palliative, local remedies was embodied in the most primitive, as well as modern, concepts of arthritis. Treat-

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ments such as liniments, packs, hydrotherapy and physiotherapy in all its forms, are time-worn remedies based on this universally accepted principle. Although possessing definite value in ordinary situations these established measures at times prove inadequate for severe or intractable complaints. In considering this subject several years ago, we felt that local injections at the site of pain or irritability, at the point of pain radiation, or, finally, at the source of nerve supply to the involved part might be a helpful and logical procedure. Such an approach is not entirely new. Among others, the late J. B. Murphy [1] of Chicago, a number of years ago, injected a 2 per cent solution of formalin in glycerine into arthritic joints, particularly when effusion was present. Charles H. Mayo [1] used a 5 per cent solution of iodoform in olive oil for injection of the osteoarthritic hip. Some 30 years ago, Morris [2] devised a special preparation for injection into affected knees. In Europe various fatty preparations are being introduced into osteoarthritic joints.[6]

Comprehensive, interesting work in this direction has been published by Forestier,[4] who employed lipiodol for periarthritic, perineural, periosseous, paravertebral, and intrarticular injections. He has reported satisfactory relief of pain by this method, notably in osteoarthritis and the various neuritides. A variety [5] of other substances have been used and advocated in this form of local and regional injection therapy,—urea and quinine solution, hypertonic dextrose solution, salines, methylthionine chloride, camphor, antipyrine, sulfur, iodine, pitcher plant extract, formic acid, alcohol, and a host of complex anesthetic formulae with some of which we have had limited or unsatisfactory experience. Deep roentgen-ray therapy [5] has given variable results.

As a result of our investigation of a number of preparations at the beginning of this work, we decided to limit our observations to procaine solution, 1 to 2 per cent, because of the reliable and consistent, though brief, response we obtained with practically no adverse effects. It is pertinent to add here that similar, favorable results have been reported abroad in the use of aqueous procaine solution, most extensively by Leriche and his coworkers,[6] de Sèze,[6] and others [6] in traumatic arthritis and in many traumatic, rheumatoid and degenerative, skeletal conditions.

As we proceeded, however, it became apparent that a substance with more prolonged action than aqueous procaine solution was desirable in some cases. We, therefore, instituted the study of 2 per cent procaine base in oil. We found this oily preparation an improvement over the aqueous in some procedures and have continued its use. The value of an oily medium in slowing absorption of the anesthetic agent and in that way prolonging analgesia has been described,[7] particularly in rectal surgery,[8] where resort to a variety of oil-soluble anesthetics has become widespread.

The Effect of Local Injections

Our observations have led us to believe that local and regional injection therapy has the advantage of permitting the application of analgesic medication close to, or at, the exact site of pain or irritation, or at the source of nerve supply and pain radiation in arthralgias and related painful states.

We have noted 1 to 2 hours of local anesthesia and from 1 to 3 days of varying degrees of analgesia when aqueous procaine solution has been administered at the proper location with correct technic. The effects of procaine in oil appear to be similar to those of the aqueous solution with greater duration. The oily preparation produces, roughly, at least one and one-half to twice as long a period of analgesia. When the pain returns after treatment, usually with diminished intensity, the site is reinjected and the procedure may have to be repeated at intervals of 3 to 5 days to 2 to 3 weeks, depending upon the severity of the complaint. In severe acute, or chronic, conditions local injection daily may be required for several treatments.

We have injected some patients once and a few 10 to 12 times before lasting relief was accomplished. The aqueous solution may always be employed, but the oil is sometimes contraindicated, as in brachial plexus block. The oily solution in many of the patients produces a local inflammatory, foreign body reaction of varying degree for 1 to 3 days. Occasionally a transient systemic reaction with slight fever may follow.

The sedimentation rate and blood picture appear to be uninfluenced by analgesic therapy.

Method

Procaine solution, aqueous or oily, has been employed by us for several years in selected cases for periarticular, intramuscular, intraligamentary, perineural, intraneural, paravertebral, caudal and a variety of other local injections at the site of pain or at the source of innervation to the painful part. Like others we have found these procedures valuable in a number of acute, painful, skeletal conditions. This report includes, however, only patients with chronic ailments in which treatment by diverse, established measures by ourselves or elsewhere in most cases had failed to give adequate relief.

This study was initiated, and most of the patients were treated, in the Arthritis Clinic of the Fourth Medical Division, Bellevue Hospital; the remainder were injected in the Arthritis Clinic of the N. Y. Post-Graduate Hospital, and in private practice. The present report embraces a variety of pathological sites and, therefore, a number of different technical approaches. The therapy described involves basically the application of accepted regional anesthetic methods to the relief of arthritis and related pain. Wherever possible, we have studied simple, local means of approach offering prospects of general usefulness.

Indications for Analgesic Injections

The therapeutic procedures under discussion are indicated when, after thorough physical examination and study, visceral disease has been ruled out as the source of pain. In such situations regional and local injections are a valuable adjunct, when the usual measures have failed to provide adequate comfort. In traumatic, rheumatoid, or degenerative processes of joints, periarticular tissues, nerves, bursae and muscles, correct injection therapy offers a promising final resort. As a preliminary measure before employing drastic surgery for intractable pain, repeated regional or local analgesic injection, or finally alcohol block, should be considered in some cases.

Contraindications

Regional and local injection therapy with analgesic solutions or alcohol should not be employed if preferable surgical measures, as a result, would be delayed. Uncontrolled diabetics are not suitable subjects. Local injections should not be administered at proposed sites which are infected or located adjacent to an area of infection; in fact, great caution or postponement is advisable when infection is present in any part of an involved extremity. Patients in extremis, or even severely debilitated individuals, should not receive regional or local analgesia if a minor shock is likely to hasten death. Great care must be exercised, and the results carefully evaluated, when injecting extremely apprehensive or neurasthenic individuals in whom a great part of the symptomatology arises from emotional or psychological factors. Psychalgia [10] must first be ruled out in these cases. Patients known to be sensitive to procaine or its derivatives should receive other treatment. A promising substitute recently developed, and effective in our experience so far, is beta-diethylaminoethyl, *p*-ethoxy benzoate hydrochloride, which is reported [2] to have the further advantage of twice the anesthetic duration of procaine hydrochloride.

The local procedures considered here may be followed safely by any practitioner thoroughly familiar with the anatomy and the method detailed, with due regard for the indications, contraindications and precautions already discussed. Paravertebral and brachial plexus block should be employed only by those trained in the technic of regional anesthesia.

Precautions in Giving Regional and Local Injections

The patient should be in a calm and comfortable position to assure relaxation of the musculature. We employ routine preliminary sedation with phenobarbital, a 1½ grain tablet administered orally 20 to 30 minutes before treatment.

In these injections, as Dutton and Lake [9] emphasize, regurgitation of solution along the needle track is avoided by using the smallest gauge needle

adequate for the occasion, by quick withdrawal of the needle, and by immediate application of pressure over the site, followed by gentle massage for 1 to 2 minutes.

Aspiration always is made before injecting and is repeated intermittently during administration, to be sure the needle has not entered a blood vessel; if blood returns, the needle is withdrawn and gentle pressure used for several minutes. The puncture is repeated then at a short distance from the first point of penetration and the treatment completed in a similar way. An injection given too superficially will be followed by bulging and may alarm the patient unless previous warning has been given.

After-pains for several hours or longer at times may follow injection. They are due usually to excessive trauma in passage and manipulation of the needle, or they may arise from back-flow of the medication infiltrating and irritating superficial tissues. After-pains are relieved by local heat with an electric pad, hot water bottle, or warm baths followed by gentle massage.

The injecting needle should always be inserted slowly and gently with a minimum of manipulation to avoid traumatizing tissues, especially blood vessels and nerves. Occasionally, when these precautions are not observed, a needle-point is broken and imbedded in the periosteum.

Surgical precautions as to sterility should be exercised at all times.

Aqueous procaine solutions may be used at room temperature, and should be fresh. We do not add adrenalin. Oily preparations are best heated to body temperature to decrease viscosity and enhance their flow. While aqueous solutions may be injected superficially, oily preparations should always be administered deeply.

Materials

We have prepared our own solutions of sterile procaine hydrochloride, 1 to 2 per cent, in normal saline freshly as needed. When small amounts are injected, up to 20 c.c., the 2 per cent solution is employed. The oily solution we use consists of procaine base, the only oil-soluble form, in sweet almond oil, dissolved in the hot oil after it is sterilized. One half to a 5 c.c. maximum of the oil may be used for injection at any particular site. The larger doses are best employed for divided, fanwise administration about a painful site to avoid undue local reaction. We have studied several of the new local anesthetic agents and a number of our own formulae which are not included in this discussion because our investigations so far are not sufficiently extensive to report.

Rustless steel needles of the beaded hilt, " Security " type should be used. The average gauge for general utility is 22. The length required may be from 1 to 5 inches depending on the place treated. Short hypodermic needles are required, of course, for the preliminary intracutaneous skin wheal at the painful area preceding every deep injection.

The regular, long 2 c.c. and 10 c.c. syringes are adequate. Barrel

flanges are helpful. The Luer lock attachment will serve for the aqueous solutions but makes oil injection difficult.

Brachial Plexus Block for the Painful Shoulder

The brachial plexus block in painful conditions of the shoulder region with aqueous procaine solution, as indicated in a previous report,[12] proved highly effective. The aqueous preparation seems adequate and its benefits of longer duration in this locality, probably because of the ease with which the medication is deposited at the nerve plexus. Owing to the delicate features of the anatomical structures we have not used the oily substance in this region.

The plexus block has been utilized as a routine measure in all intractable, non-operable disturbances of the shoulder region,—fibrositis, neuritis, bursitis and arthritis. Many painful pathological conditions of the shoulder area dependent on the brachial branches for nerve supply appear to be amenable to this form of therapy. A small percentage of cases are refractory to local procaine infiltration, even with the best technic. Painful acute and chronic involvement of the elbows, wrists and digital joints have been effectively relieved by this route but are not included in our report. We have employed, with slightly modified technic, the supraclavicular block of Labat,[13] as in figure 1.

Periarticular Injection of the Knee

The knee was one of the most commonly treated sites. As a weight bearing joint, when invaded by arthritic changes, usually osteoarthritis, it is often a source of severe pain. This discomfort arises as a rule from irritated nerve fibers supplying strained or infiltrated periarticular tissues, tendons and ligaments, particularly at their insertions and attachments. Further weakening and relaxation of the fibrous supportive structures of the joint by the intrinsic disease process leads to defective mobility, increases stress and muscle spasm with their attendant malaise.

When injecting the knee, the sore sites are determined by deep pressure against the underlying bone and, at the points of maximum tenderness, intracutaneous wheals are made with aqueous procaine solution. Injection of 2 to 5 c.c. of aqueous procaine solution is then made over, and down to, the bony contact points, usually as indicated in figure 2. If the patient is sufficiently improved, the aqueous solution may be repeated until lasting relief results. If the comfort is too brief, the oily preparation, 1 to 2 c.c. at each site, is given at the next sitting. For complete injection of the joint, we have utilized the seven point scheme of Forestier (figure 2) in 2 to 3 sessions. This method includes all of the likely tender points found about the knee.

Intraarticular injection sometimes occurs by this technic and produces

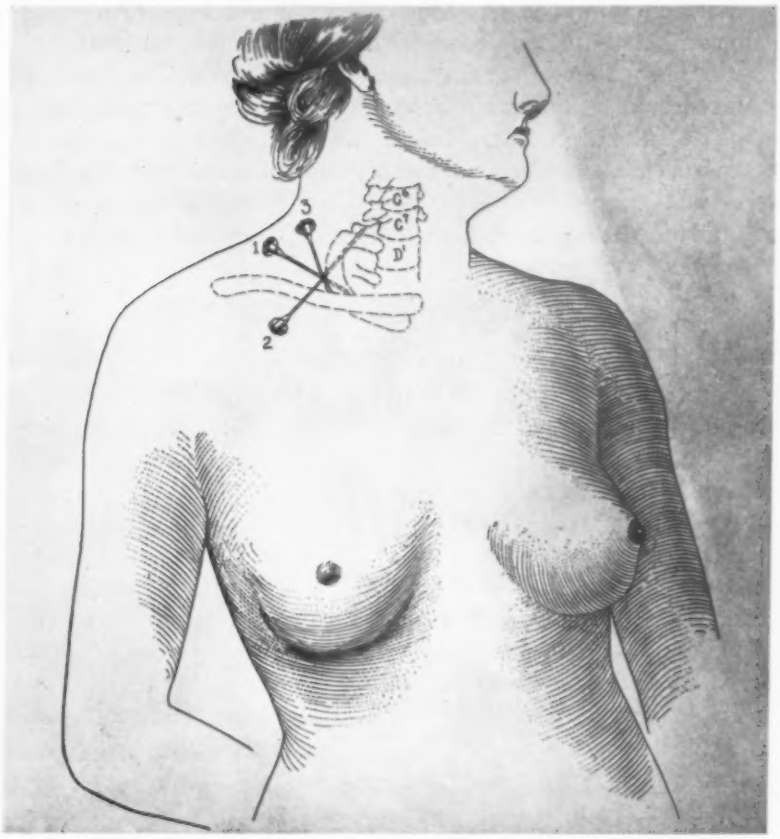

FIG. 1. Brachial plexus block by the supraclavicular route. The three directions of the needle: (1) aims at the first rib; (2) at the transverse process of C^6; (3) at the posterior margin of the first rib, behind the clavicle. (From Labat, G., Regional Anesthesia, Saunders.)

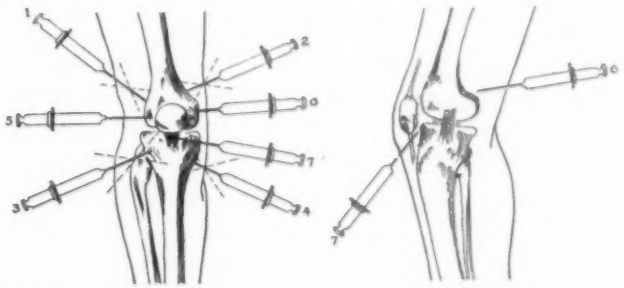

FIG. 2. Numbers 1, 2, 3, 4 and 5 are injected around the joint capsule; number 6 is made in the popliteal fossa near the cruciate ligaments; number 7 is made under the patellar ligaments. (Forestier, J., South. Med. Jr., April, 1935.)

little or no reaction if aqueous procaine solution has been employed. With the oily solution, however, an acute chemical arthritis with signs of inflammation and effusion appears in 6 to 12 hours and subsides in 3 to 6 days ordinarily. The patient should always be warned in advance of this possibility and should be informed of its temporary nature and instructed as to what to do for relief. Our experience with intraarticular therapy with a variety of preparations has demonstrated that some degree of local, and possibly systemic, reaction is likely to follow. Small doses of oil (0.5 c.c.), injected into the knee and gradually increased, were fairly well tolerated by several patients.

Periosseous Injections

Injections about painful, bony processes, particularly osteoarthritic spurs, are useful when operation is refused or must be deferred. In fact, such procedures might well be utilized as preliminary measures before subjecting some patients to surgery. If sufficient relief is obtained by periodic injection of the painful site, the discomfort eventually may not reappear. Chronic talalgias are injected at the region of the exostosis as indicated by roentgen-ray or fluoroscopy. The osteophyte may be approached from whichever aspect of the foot offers the shortest route. A subcutaneous wheal is made and the needle pierces down to periosteum (figure 3). One-half to 3 c.c. of oily solution are injected at and about the spur, followed by gentle massage for 1 to 2 minutes. There follows a local reaction of tenderness and swelling which may last one to three days and imposes some limitation on walking. Like Forestier,[4] we have observed in some cases gratifying results from medicated oil and aqueous solutions administered for painful hallux valgus and severe metatarsalgias and deposited at the bony seat of pain in these localities (figure 3).

Sacro-Iliac Region

For sacro-iliac pains not responding to the usual measures, local injection is a worthy adjunct. A procaine wheal is made at a point just medial to the margin of the posterior superior iliac spine and the needle is thrust 1 to 3 inches deep until bone is struck. Twenty c.c. of 2 per cent aqueous procaine solution or 5 c.c. of procaine in oil are deposited in three fanwise divided injections into the soft tissues over the joint, as in figure 4 (B).

Paravertebral Injections

Cervical, dorsal, lumbar, transsacral and caudal injections were employed where definite nerve localization was present. The methods described by Labat [13] were followed. The operator must be properly trained in the technic of these procedures. They constitute the logical and most effective approach in herpes zoster, neuralgia, neuropathy, arthritis of the

spine, metastases to the spine and in any parietal pain not responding to local injection at the painful site. Our experience has proved that repeated paravertebral injections of procaine solution, aqueous or oily, deposited at one or more points will adequately relieve most of the prolonged, painful conditions of selected cases of arthritis and related diseases. Finally, in intractable cases, alcohol injection can still be done by the paravertebral route, or in the extreme situation neurosurgery may be required for relief. Deep roentgen-ray therapy is being employed with favorable results in some intractable neuropathies.[5]

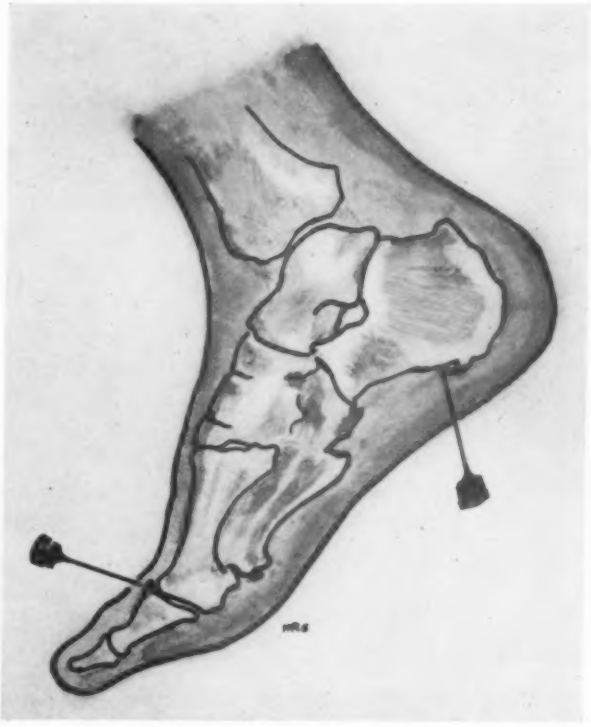

FIG. 3. Method of injecting painful spurs and osteophytes of foot.

SCIATIC NERVE INJECTION

Large nerves may be injected peripherally. Most commonly the sciatic nerve is involved and in this condition the peripheral, perineural or intraneural injection is frequently helpful. These procedures are performed preferably at the sciatic foramen. We have employed a modification of the technic described by Strauss[14] and others.

As in figure 4A, the patient lies in a lateral position, the side to be treated uppermost, the higher thigh flexed. A line is drawn joining the posterior superior iliac spine to the greater femoral trochanter at its supero-

posterior prominence. A perpendicular at the midpoint of this line is drawn and at a point 1½ inches along this perpendicular the injection is given. Following an intradermal wheal, a 4 to 5 inch needle is inserted through skin and muscle directed anteriorly and slightly medially. When the needle pierces the nerve, paresthesia is elicited. Frequently gluteal spasm is a visible accompaniment. Often the needle first impinges on iliac bone. A little gentle manoeuvering of the needle is then required until the nerve sheath is penetrated and paresthesia provoked.

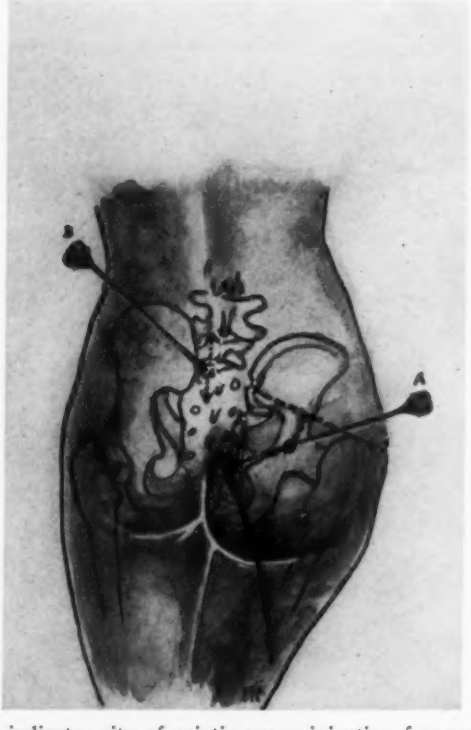

FIG. 4. Needle A indicates site of sciatic nerve injection for perineural or intraneural therapy. Needle B shows method of fanwise injection for pain about the sacro-iliac region.

For intraneural analgesia the solution is injected at this point. For perineural administration the needle is slightly withdrawn, and 10 to 30 c.c. of aqueous 1 to 2 per cent procaine solution, or 5 c.c. of oil, are injected about the nerve area. Good results have been reported from intraneural injections. We prefer the extraneural method ordinarily. When adhesions within the nerve sheath are suspected, intraneural injection of 10 c.c. of procaine, 2 per cent, followed by 50 to 75 c.c. of warm, normal saline may be given effectively.

Caudal injection of aqueous and oily medication has been so amply described in the literature [15] that it will be omitted in this discussion. We have

used the epidural technic in those patients who fail to benefit by peripheral, truncal injection. In a limited number of cases when both of these procedures prove inadequate, paravertebral block of the lumbar and sacral nerves becomes necessary.

Muscular and Fibrous Tissue Injections

The site of maximum tenderness is determined by inspection, manipulation, exercise and deep palpation. There may be several areas of preponderant tenderness as shown in figure 8. For effective therapy the examiner must recognize and inject the actual source of pain and radiation, rather than areas of reflex tenderness which are relieved spontaneously when the focal points are blocked. Having determined these points, or the point,

Fig. 5. Periarticular injection of knee at tender points with iodized oil.

for injection, one or more superficial wheals are made, and with a 2 to 3 inch needle, 5 to 20 c.c. of aqueous solution or 1 to 5 c.c. of oil are injected directly into the site of pain and tenderness.

We have found this procedure of great value in traumatic and infectious conditions, especially in fibrositis of the erector spinae, gluteal and thigh muscles; about the fascia lata, lumbo-sacral and sacro-iliac ligaments in back pain. If painful, sharply circumscribed, subcutaneous or intramuscular nodules are palpable, they are penetrated with the needle and 5 to 10 drops of the solution are injected into the center of the nodule, the treatment then being completed with radiating fractional deposits of 3 to 5 c.c. of aqueous or oily solution about and beyond the nodule. If a nodule is persistently

and exquisitely tender, 3 to 6 mm. of 95 per cent alcohol are injected into the nodule and 5 c.c. aqueous solution about the site of pain.

In widespread fibrositic involvement of fascia or muscles, particularly in the gluteal and low back regions, we have resorted to deep, massive injections of 10 c.c. of 2 per cent procaine with 25 to 100 c.c. of normal saline. This method appears to exercise its benefits by breaking up adhesions as well as by the analgesic action of procaine and of volume pressure. Tenderness and crepitation frequently disappear after 1 to 2 such treatments.

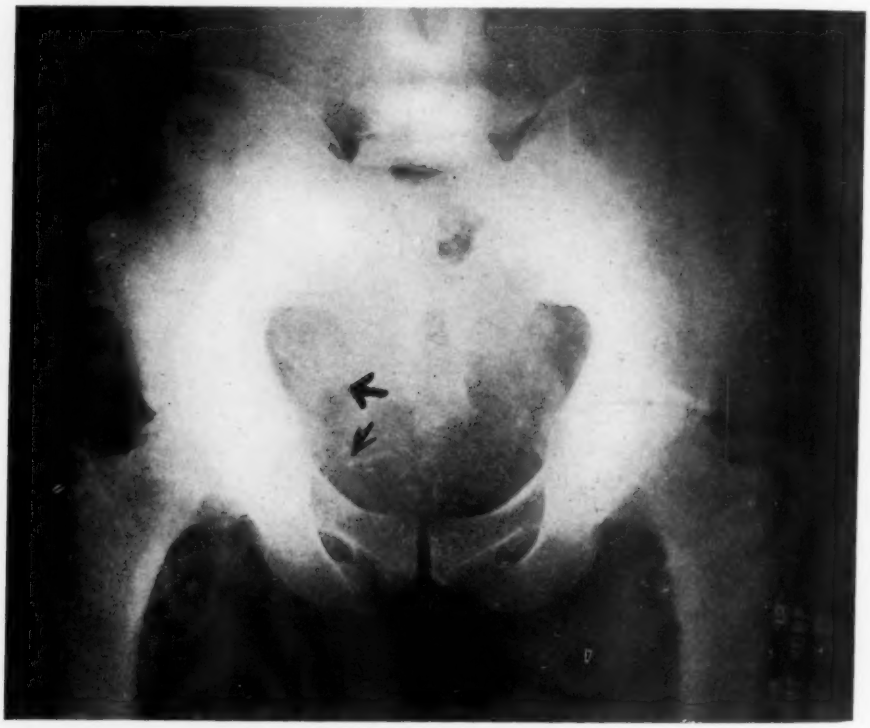

FIG. 6. Perineural and intraneural injection of sciatic nerve with brominized oil.

Relief in acute traumatic and fibrositic ("lumbago") back pain has been reported[16] recently by injection of aqueous procaine solution. In chronic fibrositis, especially with muscular and fascial nodulation, Maliwa[16] advocates the administration of small doses of procaine solution in situ.

HAZARDS IN REGIONAL AND LOCAL INJECTIONS

In our experience with several hundred regional and local injections, we have seen only one severe mishap. A patient with known coronary disease, 70 years of age, was given brachial plexus block without proper inquiry into her general condition. Following only the intracutaneous wheal she fainted.

When the patient was studied in the ward, we found that there was a very definite history suggestive of impending coronary occlusion during the morning preceding the treatment. A lesser complication which occurred once was the formation of a sterile chemical abscess over the sacro-iliac region in a lean subject when an irritating, halogenized oil solution was incorrectly injected subcutaneously, practically between skin and bone. The abscess was arrested spontaneously after two aspirations.

Obviously brachial plexus block is subject to the possibility of perforation of any of the adjacent large blood vessels. Occasionally this accident occurs in our hands and appears inconsequential provided repeated aspiration forms part of the operator's technic, so that he recognizes the vascular penetration before the medication is injected. If small amounts of aqueous procaine solution enter a vessel, no complications are likely, since procaine preparations evidently are administered intravenously with impunity.[17] Puncture of apical pleura or lung may occur but has not happened in our experience.

FIG. 7. Sacro-iliac block visualized with brominized oil by fanwise injection.

While we have noted excellent results in some patients receiving intra-articular injection, it strikes us as unnecessary to enter a joint space unless periarticular inoculation has failed to provide relief. We did employ the intraarticular route in some cases of severe osteoarthritis of the knee in which the pathologic changes seemed too far advanced for any added injury to arise. At this time, however, we feel that the arthritic changes produced in animals by introducing into the joints a variety of innocuous substances, including physiological saline and distilled water,[18] should discourage indiscriminate intraarticular instillations excepting in advanced lesions or when a joint must be entered anyhow to remove an effusion.

In the course of perineural and intraneural injection, indelicate technic may lead to injury of nerve tissue, productive of troublesome paresthesia.

Intraneural procedures are usually avoided by us because of this possible hazard. They should be reserved for the large sciatic trunk when intrathecal adhesions are suspected. Employment of large volumes of fluid, with procaine and saline, for intraneural, perineural, intramuscular and extrafascial infiltration, despite their extensive use, appears to be free from the

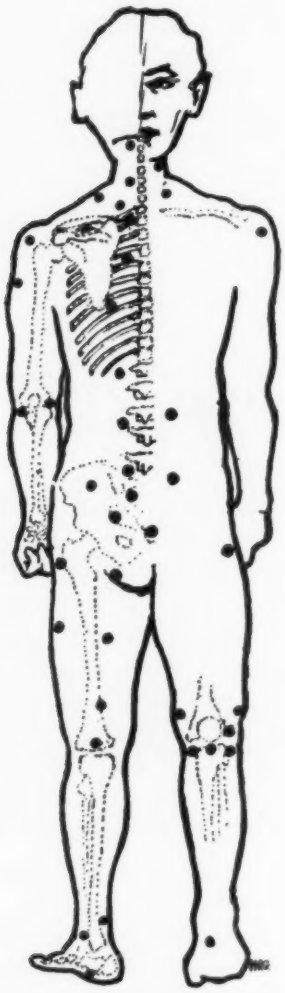

FIG. 8. Common focal points of pain and tenderness on palpation in neuralgic and myalgic (fibrositic) states. At these points local analgesic injection is given.

nerve disturbances reported by Hassin.[19] We have noticed no evidence of persistent infiltration or proliferation at sites repeatedly blocked with procaine solutions. These changes are known to occur following injections of quinine derivatives and were observed by us in five patients who had received such treatment.

Results

The patients in this study were under our observation from six weeks to eleven months. Almost all of them were coöperative enough to attend our clinic for a minimum period of three months to permit us to watch closely the effects of therapy. In estimating our results we were guided by the subjective relief of pain and stiffness and the objective changes in tenderness, muscle spasm and mobility of the part. Improvement was considered moderate when pain ceased and 50 to 70 per cent recovery of function occurred. Great to complete improvement was evidenced by functional recovery of 70 to 100 per cent as well as by the absence of pain.

As table 1 indicates, the number of patients treated with brachial plexus block for painful shoulder conditions has increased since a preliminary re-

Table I

Results of Local and Regional Injections

No. Cases Treated	Brachial Plexus Block	Direct Bursa Inject.	Para-vertebral Block		Inject. Sciatic Trunk	Intra-artic. Injection		Peri-artic. Inject.	Local Inject. for Fibrositis Low Back
			Proc.	Oil		Proc.	Oil		
134	42	13	12	9	9	13	5	16	15
Unimproved	6	6	2		1	6	2	3	2
Slightly improved	2				2	2		2	
Moderately improved	4			4	2	2	1	2	3
Greatly or entirely improved	30	7	10	5	4	3	2	9	10
Average number injections	5.5	3.3	3.7	1.7	5.2	2	1	5.9	6.7
Duration of disease	2 mos. to 7 yrs.	3 mos. to 8 yrs.	3½ mos. to 7 yrs.	9 wks. to 8 yrs.	9 mos. to 5 yrs.	2½ mos. to 15 yrs.	1–5 yrs.	1–4 yrs.	3 mos. to 4 yrs.

port [12] to 42. This group represents a variety of pathological states; in it 32 patients, or 80.9 per cent, were moderately to entirely relieved; 4.7 per cent only slightly improved, and 14.3 per cent unimproved.

Of 13 patients receiving direct injection into the subdeltoid bursa, seven were improved and six were not benefited. This procedure has not demonstrated in our hands the effectiveness shown by brachial plexus block in bursal disease of the shoulder region.

Intraarticular administration of aqueous procaine solution in the early stages of our clinical investigation failed in seven of 13 patients and gave slight relief in two. Two of five patients receiving the oily solution showed great improvement.

Periarticular injection, chiefly of the knee joint, elicited complete or

moderate improvement in 11 of 16 patients, slight improvement in two and none in three patients.

Perineural deposit of solution at the sciatic trunk in nine patients gave complete improvement in four, slight benefit in two patients and none in another. Two patients were moderately improved.

Local injection for fibrositis was performed in 15 patients, all with involvement of the low back or gluteal areas. Ten cases responded with great or complete improvement, three were moderately benefited, while two patients were unrelieved.

Paravertebral block proved greatly or completely effective in 10 of 12 patients receiving aqueous procaine solution. Of nine patients treated with the oily preparation all were moderately, greatly or completely benefited. The paravertebral route was the most effective approach employed in this study. It appears to be, on anatomical, physiological and anesthetic principles, the most useful procedure for relief of the painful conditions presented here. We have employed the peripheral methods of injection at some pain sites, as previously stated, in order to evaluate their utility. The peripheral, local injection requiring no specially trained technic and offering a simple approach, nevertheless, may often prove, according to our results, a valuable adjunct in the management of arthralgia and related painful states.

The series of 134 patients showed great or complete improvement in 59.7 per cent, moderate improvement in 13.4 per cent, slight improvement in 5.9 per cent, no improvement in 20.9 per cent. Of the latter group of (28) unimproved patients, nine failed to appear after the first treatment. While we have had a number of recoveries following one injection, we considered treatments as failures, for the sake of conservative evaluation, if the patient failed to return for further injections or follow-up after the first block.

The average number of injections varied with the locality treated as shown in table 1. A limited number of patients were injected at some sites. We feel that inclusion of these small groups in our study is justified by the fact that we are reporting the results of the application of basic principles common to all of the treatments at the various locations.

It is interesting to note that only two patients presented such severe symptoms, unresponsive to procaine analgesia, that paravertebral block with alcohol was required and was permitted. Our experience suggests that the pain in arthritic and allied conditions, even when protracted and severe, yields frequently to repeated procaine injection.

The patients reported in this series usually were given no other form of analgesic therapy in order that the results of block treatment could be properly evaluated. Undoubtedly, as we have observed in our private patients, when these analgesic procedures supplement suitable medical, physiotherapeutic and orthopedic measures, as they should under ordinary circumstances, a smoother, briefer period of treatment may be expected. Manipulation and local supportive devices such as bandages and casts are tolerated better, and

prove more effective, when applied after injection therapy in these painful states. We must emphasize that analgesic injection therapy should be employed only as an accessory to the accepted medical and orthopedic management of these conditions.

Follow-Up

During preparation of this article an effort was made to obtain a report of progress by mail or by reëxamination of the patients in our study. In most of the series included here, treatment was completed from 4 months to 2½ years before compilation. We succeeded in getting acceptable information or a return visit from 19 patients. Of eight who had received brachial plexus block for shoulder conditions four months to two and one-half years earlier, all reported satisfactory and continued relief. One of these patients occasionally is subject to bouts of shoulder pain unaccompanied by disability. Two continued to have diffuse aches elsewhere, just as they did before treatment.

Of seven patients receiving periarticular injections of the knee, ten months to two years prior to our inquiry, three appeared to have continuous adequate to complete relief. Two patients, one who received periarticular procaine in oil injection of the knee eight months before reëxamination, and another who was given periarticular procaine solution three years previously, reported the same pain and disability without any improvement at any time following therapy. Two patients, treated with paravertebral procaine in oil six months and 18 months respectively before follow-up, reported persistent, complete relief.

One patient, given three perineural procaine solution injections of the sciatic nerve, after one year stated that she had felt no return of the symptoms which had been disabling for six months before nerve blocking. Following the injections, she had experienced from time to time occasional twinges of "muscular" pain but none in the region of the sciatic distribution. One patient who received two injections about a painful spur of the os calcis reported complete freedom from pain and disability at the time, five months after treatment.

Of the 19 patients answering or returning, 17, or about 90 per cent, therefore, appeared to be adequately or completely relieved of the intractable pain and disability for which they had required treatment. The intervals between treatment and check-up varied from four to 30 months. Two patients had obtained no relief immediately after injection, both receiving periarticular therapy of the knees. One was a female of 76 years with advanced osteoarthritis; the other was a male of 60 years with a severe posttraumatic and osteoarthritic condition of the treated knee of many years' duration complicated by long-standing fibrous ankylosis. Four patients who had experienced complete relief following local injections reported severe, periodic pain in other parts of the body but complete, lasting quiescence of the area treated.

Discussion

The patients reported here were treated at different painful sites for a variety of conditions, but the methods of relief were essentially identical. Our observations demonstrate, so far, that in chronic arthritis and related disease presenting prolonged, intractable discomfort, local or regional analgesic therapy offers relief, rest and relaxation for a majority of the patients.

While the treatment described is essentially palliative, the enduring relief of pain and general improvement often resulting from repeated local and regional injections of procaine solution raise the question as to the basis of the lasting response to what is expected to be transient medication. The clinical course of patients under treatment suggests a number of direct and indirect beneficial effects of regional and local analgesia.

An immediate reaction to procaine solution is, obviously, anesthesia. We have been impressed by the striking persistence of analgesia in many of these painful states after anesthesia has disappeared. With oily solutions of procaine, prolonged analgesia is especially noticeable. These observations have been confirmed by Bacon [20] of Philadelphia who has injected oil-soluble anesthetics caudally and transsacrally for rectal neoplasms and obtained 1 to 2 weeks' relief of pain when roentgen-ray and radium had failed to give adequate control of discomfort.

Another direct effect of local analgesic injection is probably a hyperemia contributed in part by the vasodilatation arising from the pharmacologic action of procaine with its anesthetization of any immediate sympathetic nerve supply. It is likely also that the injections act as a form of regional shock therapy with a local foreign body reaction and congestive response that add to the hyperemia.

Another important feature of these therapeutic injections is the relaxation of reflex muscular spasm and prevention of atrophy following the resulting disuse when prolonged. The release of spasm sometimes appears immediately after treatment and becomes more pronounced and maintained as the injections are repeated. Abnormal postural tendencies are to some extent corrected reflexly following relief. Further functional improvement is afforded by the manipulative procedures which then are permitted. Normal mobility becomes possible in many cases where joint function had been limited for some time. Systemic response to eradication of pain and local relaxation is evidenced by the improved well-being of the patient, allowing rest and sleep which frequently are disturbed. The patient's outlook and morale are stimulated by what is often the first appreciable relief in an extended period of discomfort and disability.

These observations concerning the effects of analgesic block on reflex, spastic, and eventually atrophic, changes associated with such prolonged, painful states are supported by the work of Reymond [21] years ago. As May [21] reports, "by injecting silver nitrate and turpentine into the knee joints of dogs, he (Reymond) produced suppurative arthritis and noted the

appearance of the atrophic changes and exaggerated reflexes associated with the chronic arthritis of humans. However, muscular atrophy requires for its production an intact reflex arc; if it is broken, he found, for example by sectioning the posterior roots, muscular atrophy does not occur." Local analgesia permits a temporary interruption of the sensory reflex at the painful, involved area.

An added source of benefit upon which we may speculate is the probable elevation, or modification, of the threshold of pain in these patients when prolonged or repeated analgesia is introduced. This change in the sensory response may be influenced by the repeated interruption of the prolonged pain-spasm cycle, as Reymond's work suggests. By a reduction in the number of pain stimuli transmitted from the pathological site after analgesic therapy, interference with the "summation of stimuli" [22] characteristic of these prolonged painful states may occur. Furthermore, some effect upon the local tissue metabolism may well be initiated by the local analgesia, hyperemia and rest.

There are mechanical effects of local injections which probably play a part in the improvement achieved. The administration of large volumes of fluid, by separating contiguous tissues and stretching or breaking fine adhesions, may add to the intrinsic value of the medication, especially in fibrositis and in periarticular pathologic lesions. When the oily solutions are employed, there may be some further lubricant value in such a medium, probably at the movable surfaces of muscles, bursae, tendons and joint structures where palpable crepitation suggests roughening of adjacent tissues.

In the disorders considered here, the well-known tendency of long inactive joints and muscles toward disuse atrophy is commonly observed. Whether the patient actually feels pain on movement or merely fears pain, mobilization of these structures often can be induced for the first time and maintained by local or regional analgesia with procaine solutions. Certainly in protracted, painful articular and related disorders, when they fail to respond to the usual methods of management, a form of treatment frequently offering lasting relief of discomfort and its associated disability should prove a worthy adjunct to our therapeutic resources. The effectiveness of local and regional analgesic injection in our group so far warrants more extensive clinical and other investigation of this form of therapy in painful, disabling rheumatic disease.

The chief limitation of local and regional analgesia at the present time, apart from paravertebral alcohol block, is the necessity in many patients of repeated injection in order to maintain prolonged relief of pain until adequate recovery is accomplished. The present trend in the development of local anesthetics promises in the near future the production of an agent with the advantages of prolonged analgesia and low toxicity. When such a substance becomes available and is applied by the various technics discussed, we will have a potent remedy requiring fewer injections for the control of

disabling pain in a still higher percentage of arthritics than we are able to report at this time. As a last resort, for the present, in those situations where milder analgesia is ineffective or requires too frequent repetition, there still remains alcohol block of the nerve supply to the painful part by the paravertebral route.

Conclusions

We are aware of the tendency of rheumatic disease to show spontaneous remissions. Since almost all of the patients, however, had received for some time previously other accepted measures without relief, this previous period of therapy was available in these cases as a control. The follow-up information, even though limited to 19 cases, indicates at least that the immediate relief offered by local and regional injections is sustained for long intervals in many of the patients. More precise evaluation will have to await further lapse of time and additional experience with these procedures. Therapy was more effective at some sites than at others, due, we believe, to varying difficulties of technic at different areas. From our observations in the treatment of the group reported here and from the information elicited by our follow-up study, the following conclusions may be stated:

(1) Repeated injection with aqueous and oily solutions of procaine according to accepted anesthetic methods, at the site of pain or at the source of nerve supply to the painful area in a group of 134 patients with chronic, intractable discomfort, gave poor, or no, results in 20.9 per cent of the patients; slight improvement in 5.9 per cent; moderate relief in 13.4 per cent and complete, lasting relief of pain in 59.7 per cent of the patients, a total of 73.1 per cent of the patients experiencing moderate to complete relief.

(2) Follow-up of 19 patients from 4 to 30 months after treatment revealed 17 still adequately or completely relieved; two unrelieved.

(3) The treatment of intractable arthralgia and allied painful states by local or regional analgesic injection offers a promising, palliative, accessory therapeutic measure in arthritis and related conditions.

Table II

	Number of Patients	Percentage
Unimproved	28	20.9
Slightly improved	8	5.9
Moderately improved	18	13.4
Greatly improved or fully recovered	80	59.7
Total patients treated	134	
Total, slight or no improvement	36	26.8
Total moderately to entirely improved	87	73.1

I wish to acknowledge the assistance in the conduct of this study given by the staffs of the Arthritis Clinics of the N. Y. Post-Graduate Medical School and Hospital and of Bellevue Hospital, 4th Division, particularly by Drs. Freeman Brooks, Edward E. P. La Motta, Saul Solomon and James M. Tarsy. Figures 3, 4, and 8 were drawn by Harry R. Greenburgh, D.D.S. Special preparations were supplied by Abbott Laboratories, Rare Chemicals, Inc. and E. R. Squibb and Sons.

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THE SIGNIFICANCE OF GASTRIC ACIDITY AFTER HISTAMINE STIMULATION: A STATISTICAL STUDY OF 2877 GASTRIC ANALYSES *

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MOST of the reports of gastric analyses which have appeared previously in the literature [1, 2, 3] are based upon values obtained after a test meal of the Ewald type. It is well known that the administration of histamine is the most reliable method of evoking gastric secretion.[4, 5] Since the opening of Duke Hospital in 1930 all gastric analyses here have been made with the use of this drug, and examinations of the contents of the stomach by this method have been made in 3675 patients. It seems profitable, therefore, to examine these data critically in order to determine whether acid values obtained with histamine stimulation vary materially from those obtained with the Ewald meal, and to evaluate, if possible, the significance of a single gastric analysis in the diagnosis of disease.

Method of Gastric Analysis. In all patients in this series the gastric analysis was done according to the following routine:

1. Fasting contents were withdrawn from the stomach.
2. 50 c.c. of 7 per cent ethyl alcohol were then given to the patient by mouth.
3. 0.5 mg. of histamine acid phosphate was given subcutaneously.
4. At the end of 45 minutes the contents of the stomach were withdrawn and titrated against N/10 NaOH, using Töpfer's reagent and phenolphthalein. The analysis of free acid only is reported.

Material. This study is based upon the acid values obtained in 2877 patients. Of this group, 1917 patients showed no evidence of disease after thorough study, *including a roentgenological examination of the gastrointestinal tract.* These were used as normal controls. The analyses in those patients who had no roentgenological studies were discarded, even though there was no clinical evidence of disease. It is believed, therefore, that those patients classified as normal controls actually had no organic disease. All patients with systemic disease, such as syphilis, tuberculosis, hypertension, nephritis, and heart disease were excluded, and the results of gastric analyses in the following disease groups were selected for study: *duodenal ulcer, gastric ulcer, carcinoma of the stomach, chronic cholecystitis, pellagra, rheumatoid arthritis,* and *hypertrophic arthritis.* The diagnosis of

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duodenal or gastric ulcer, gastric carcinoma and chronic cholecystitis was confirmed in every case by roentgenological studies or by operation.

The distribution of the data under consideration is summarized in table 1. Since the analysis is concerned with the acid values of patients showing free acid, all patients with achlorhydria will be considered separately.

TABLE I

Distribution of Cases

	Number Showing Free HCl	Number With Achlorhydria		Total
		No.	%	
Normal controls	1706	211	11.0	1917
Duodenal ulcer	419	24	5.4	443
Gastric ulcer	42	3	6.7	45
Carcinoma of stomach	37	48	56.5	85
Chronic cholecystitis	92	38	29.2	130
Pellagra	53	50	48.5	103
Rheumatoid arthritis	51	9	15.0	60
Hypertrophic arthritis	79	15	16.0	94
TOTALS	2479	398		2877

Range of Free HCl in Normal Controls. Tables 2 and 2a summarize the findings in this group according to age and sex. The number of cases in each decade was plotted against the acidity and tabulated as shown. The arithmetical means, the standard deviations from the mean and the coefficients of variation are included. The wide range in values is indicated not only by the figures in the distribution table but also by the large coefficients of variation. In two-thirds of the analyses the acid values range from 30 degrees to 85 degrees of acidity. This is shown graphically in chart 1. In the remaining cases the acid values fell outside of this wide range.

As seen in the tables and chart, the mean for females is lower than that for males for corresponding decades. This has been pointed out by Vanzant.[1] To determine whether this difference was significant the usual statistical methods[6] were employed, and the results are shown in table 3. Significant differences were found in all decades studied except in the sixth and seventh.

Gastric Acidity in Certain Diseases. The gastric acid values found in different diseases were grouped and compared with the normal standards established above. Since the number of cases in each group was relatively small, the calculations used in making table 3 were not directly applicable, and the following method, which takes into consideration both age and sex, was employed. The gastric acidity of each case was compared with the mean for the corresponding decade and sex. These positive and negative

TABLE II

Distribution of Cases in Normal Controls According to Age and Sex—Males Age

Gastric Acidity	0–10	11–20	21–30	31–40	41–50	51–60	61–70	71–80	81–90	Total	Percentage
1–10°		3	7	14	7	7				38	4.5
11–20°		3	14	17	10	8	4	2	1	59	7.0
21–30°		1	16	13	9	12	1			52	6.2
31–40°		7	26	34	14	8	9	1		99	11.8
41–50°		4	31	29	30	16	8			118	14.0
51–60°		6	26	30	27	11	6	3		109	13.0
61–70°		6	32	29	29	15	2			113	13.4
71–80°		3	28	36	16	10	2	1		96	11.4
81–90°		6	17	19	14	17	3	2		78	9.3
91–100°		4	9	14	12	7	2	1		49	5.8
101–110°		2	6	3	8	3	1			23	2.7
111–120°			2	1	3		2			8	0.9
121–130°											
TOTAL		45	214	239	179	114	40	10	1	842	
Mean.....		58.2	55.9	54.0	58.8	55.4	54.0				
Standard deviation...		27.9	22.3	25.6	25.1	28.9	26.6				
Coefficient of variation...		42	40	47	43	52	49				

TABLE IIa

Distribution of Cases in Normal Controls According to Age and Sex—Females Age

Gastric Acidity	0–10	11–20	21–30	31–40	41–50	51–60	61–70	71–80	81–90	Total	Percentage
1–10°		4	8	10	11	8	7			48	5.6
11–20°	1	4	17	22	21	15	9			89	10.3
21–30°	1	2	22	27	17	13	6			88	10.2
31–40°		3	27	34	27	27	8	2		128	14.8
41–50°		8	32	36	31	15	4			126	14.6
51–60°		5	40	38	20	23	6	3		135	15.6
61–70°	1	3	20	28	28	9	3			92	10.6
71–80°		3	11	12	13	20	3			62	7.2
81–90°			8	14	15	14	1			52	6.0
91–100°		1		5	10	2	7			25	2.9
101–110°			3	2	3	3	3			14	1.6
111–120°			1	2	1					4	0.5
121–130°							1			1	
TOTAL	3	33	189	230	197	149	58	5		864	
Mean.....		42.9	46.3	47.4	50.4	49.6	45.5				
Standard deviation...		23.1	26.2	27.7	25.9	25.2	31.3				
Coefficient of variation...		54	59	58	51	51	69				

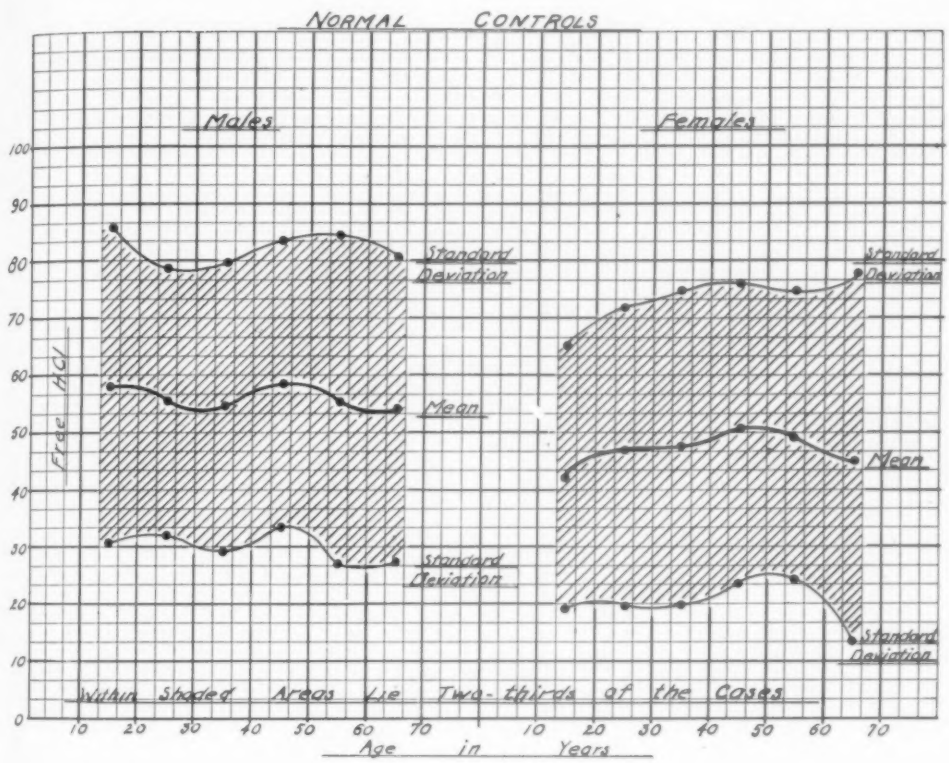

CHART 1

TABLE III

Comparison of Normal Males and Females

Age	Males			Females			Difference of Mean	Standard Error of Difference	Significance*	
	Mean	Standard Deviation	Number of Cases	Mean	Standard Deviation	Number of Cases				
11–20	58.2	27.9	45	42.9	23.1	33	15.3	5.8	2.6	Significant
21–30	55.9	22.3	214	46.3	26.2	189	9.6	2.4	4.0	Significant
31–40	54.0	25.6	239	47.4	27.7	230	6.6	2.5	2.6	Significant
41–50	58.8	25.1	179	50.4	25.9	197	8.4	2.6	3.2	Significant
51–60	55.4	28.9	114	49.6	25.2	149	5.8	3.4	1.7	Not significant
61–70	54.0	26.6	40	45.5	31.3	58	8.5	5.9	1.4	Not significant

* The figures in this column were obtained by dividing the difference of the mean by the standard error of the difference. If the value obtained is greater than 2, the difference of the means is significant as indicated in the last column.

differences were totalled. The difference of these totals was divided by the number of cases, giving the mean difference for the disease under consideration. The standard deviation of this difference was then computed and the standard error of the deviation. The results of these calculations are recorded in table 4. It will be observed that a significant variation from the

TABLE IV

Comparison of Gastric Acidity in Disease with Normal Controls

	Number of Cases	Mean Difference From Normal	Standard Deviation of Difference	Standard Error of Standard Deviation	Significance*	
Duodenal ulcer	419	+10.2	25.2	1.2	8.3	Significant
Gastric ulcer	42	− 7.3	21.8	3.4	2.1	Significant (?)
Carcinoma of stomach	37	−23.2	32.3	5.3	4.3	Significant
Chronic cholecystitis	92	− 1.4	26.2	2.7	0.5	Not significant
Pellagra	53	−12.2	25.3	3.5	3.5	Significant
Rheumatoid arthritis	51	− 2.5	22.8	3.2	0.8	Not significant
Hypertrophic arthritis	79	+ 1.2	28.0	3.1	0.4	Not significant

* See footnote of table 3.

normal was found in duodenal ulcer, carcinoma of the stomach and pellagra, but not in chronic cholecystitis, rheumatoid and hypertrophic arthritis. In duodenal ulcer only was the level of gastric acidity higher than the calculated normal; in the other diseases it was lower.

Achlorhydria. Patients showing an absence of free HCl, excluded from the group of patients studied above, were next considered. The number of patients in each group showing achlorhydria and the percentage of the total are shown in table 1. To analyze this material further, the incidence of achlorhydria in normal controls was determined for each decade and recorded in table 5. The incidence of achlorhydria in the diseases studied,

TABLE V

Achlorhydria

Males			Females		
Age	Number of Cases	Percentage	Age	Number of Cases	Percentage
0–10	0	0	0–10	0	0
11–20	0	0	11–20	0	0
21–30	10	4.5	21–30	7	3.6
31–40	21	8.4	31–40	20	8.0
41–50	27	13.1	41–50	29	12.8
51–60	32	21.9	51–60	27	15.3
61–80	18	26.5	61–80	20	24.1

shown graphically in chart 2, is highest in carcinoma of the stomach and in pellagra. It will be noted that when free HCl does occur in these diseases, the values are low. Exactly the opposite is seen in duodenal ulcer where there is a high level of gastric acidity and a low incidence of achlorhydria.

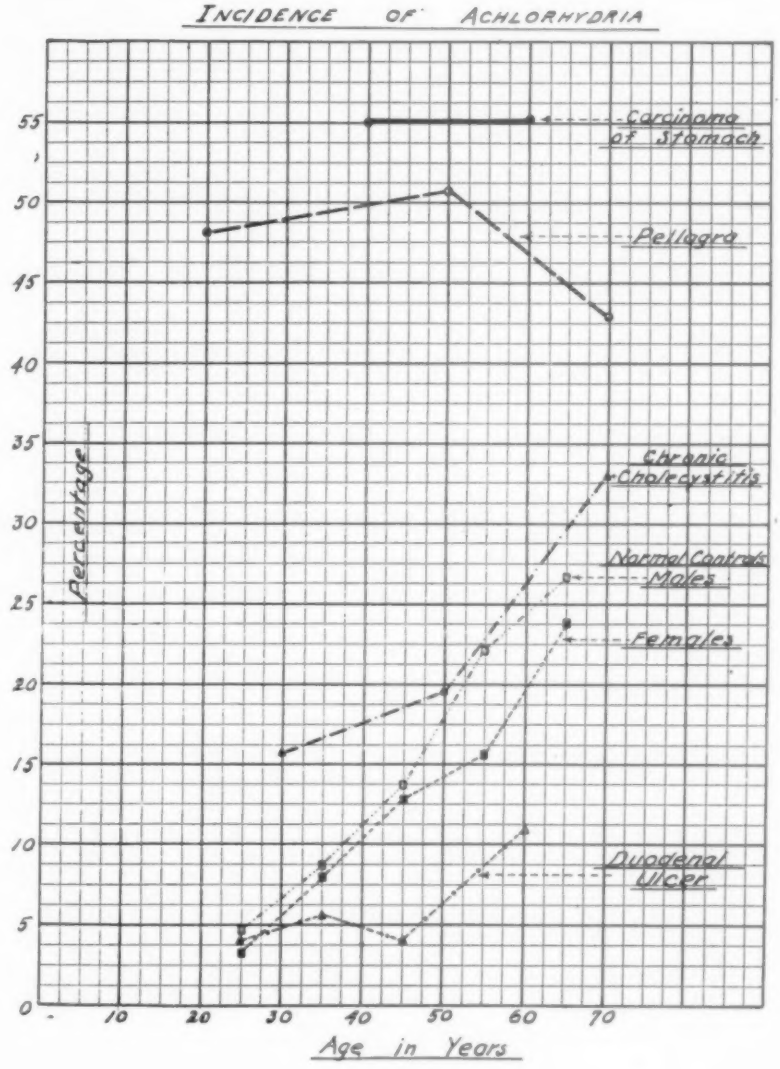

CHART 2

DISCUSSION

In most hospitals and clinics in this country an analysis of the stomach contents is a routine procedure, rarely omitted in the study of patients presenting symptoms referable to the gastrointestinal tract. Great stress

has been laid upon the amount of free HCl present. There has been some confusion as to just what values are to be taken as evidence of hyper- or hypo-acidity, but in general it is thought that the level of gastric acidity is of definite importance and a material aid in the diagnosis of disease.

In considering the excellent work of Vanzant and her co-workers [1] in establishing the normal range of gastric acidity from youth to old age, it should be pointed out that her findings are based entirely upon values obtained after the use of the Ewald type meal. In this study, on the contrary, histamine was used exclusively. It is interesting to note the close similarity in the results of these separate studies. The incidence of achlorhydria in normals in this study closely parallels that reported by her. It should be pointed out, however, that there is a much wider range of variation in normal individuals after histamine than after the Ewald meal.

From this study it is evident that one cannot assert that there is a normal level of gastric acidity. The range is far too great. As seen in chart 1, a variation of 55 degrees is found in two-thirds of the normal cases, and, of course, a much larger variation exists when all analyses are included. With such a wide range of values occurring in normal individuals, to attach any significance to the actual value of a single determination is not justifiable.

On the other hand, it is evident that a significant difference occurs between the acid values of men and women when a large number of cases is considered. Decade for decade, the mean for women is significantly lower. This does not mean that in an individual case one will necessarily find a lower value for a woman than for a man of corresponding age, but it is probable that this will be the case.

This same reasoning applies equally forcibly to the findings in the diseases studied. In duodenal ulcer it is probable that the acid value will be high; in carcinoma of the stomach and in pellagra one may reasonably expect the values to be low. However, it is clear that a high acid value may occur in either of these diseases, or a low one in duodenal ulcer.

It has been reported [7] that one finds low gastric acidities in rheumatoid arthritis. Referring to table 4, it will be seen that no significant variation from the normal was found in either rheumatoid or hypertrophic arthritis.

The incidence of achlorhydria is interesting. This has been shown by Vanzant to increase rapidly with age. The incidence in the normal controls in this series compares closely with her findings. As one would expect, the incidence of achlorhydria in carcinoma of the stomach and in pellagra is very high. It is frequently stated that achlorhydria does not occur in duodenal ulcer.[4] In this study, 24 patients (5.4 per cent) with active duodenal ulcer, proved roentgenologically, were found to have no free HCl after histamine.

Even though it has been shown that the level of free acid in a single determination is of little significance, one should not draw the conclusion that gastric analyses are useless or should be abandoned. The demonstration of achlorhydria is of sufficient importance to justify the procedure.

Conclusions

1. The range of gastric acidity after histamine stimulation in normal individuals is so great that it is impossible to determine what values are to be taken as evidence of normal acidity, hyper-, or hypo-acidity.

2. This range of values is much greater after histamine than after the Ewald meal.

3. If free HCl is present after histamine stimulation, the actual level of acidity is of little, if any, diagnostic significance.

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THE VALUE OF THE WELTMANN SERUM COAGULATION REACTION AS A LABORATORY DIAGNOSTIC AID; COMPARISON WITH THE SEDIMENTATION RATE *

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Introduction

In this report we wish to call attention to a nonspecific laboratory test which merits consideration and which we believe is often of more value than the sedimentation rate. This test, which is known as Weltmann's serum-coagulation reaction or the coagulation band of the serum, was proposed in 1930, and has attracted much favorable comment in Europe, although it has not received sufficient trial in this country. Weltmann [1] showed that by this reaction one could distinguish between exudative processes on the one hand and fibrotic processes or parenchymal liver damage on the other. Furthermore, the test is roughly quantitative and reflects the degree of exudation present.

Weltmann found that normal serum which is diluted 50 times with distilled water and then heated in a boiling water bath fails to coagulate, since the minimal concentration of electrolyte necessary for heat coagulation is not present. If sufficient electrolyte in the form of the chlorides of calcium, barium or magnesium is added to the diluted serum, it will then coagulate when heated. In certain conditions the serum was found to require greater concentrations of electrolyte than normal, whereas in others it coagulated with even smaller concentrations than normal. From these observations Weltmann evolved the following technic for his test.

Technic

A stock solution of 10 per cent $CaCl_2 \cdot 6H_2O$ is prepared and from this, 10 dilutions are made up consisting of 0.1 per cent, 0.09 per cent, 0.08 per cent, 0.07 per cent, 0.06 per cent, 0.05 per cent, 0.04 per cent, 0.03 per cent, 0.02 per cent and 0.01 per cent calcium chloride. Ten small test tubes are placed in a rack and numbered in order from 1 to 10. Into each tube is pipetted 5 c.c. of the similarly numbered $CaCl_2$ solution and 0.1 c.c. of hemoglobin-free serum. The tubes are shaken and placed in a boiling water bath for 15 minutes. They are then removed and the tubes which show

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coagulation or flocculation are noted. Coagulation always begins in the tubes with the higher concentrations of calcium chloride and stops toward the lower concentrations. That is, if there is coagulation in the fifth tube, for example, there will necessarily be coagulation in the first four tubes. The number of tubes in which coagulation occurs gives us the coagulation band of the serum. There is usually a sharp unmistakable differentiation between the last tube which shows coagulation and the next tube which may be only turbid or cloudy. Sometimes, however, there is a slight or doubtful coagulation in the intermediate tube and in such cases the coagulation band is said to be between that tube and the one before it. For example, if tube 6 has a definite coagulation and tube 8 has none, but tube 7 has a slight coagulation, the coagulation band is 6½. In normal serum the first six tubes usually show coagulation so that the normal coagulation band is 6. If the coagulation band is less than 6 the reaction shows a shift to the left, whereas if the coagulation band is greater than 6, there is a shift to the right.

Interpretation of the Weltmann Reaction

In pathological conditions the coagulation band may be normal, shortened or lengthened. Inflammatory and exudative processes were shown by Weltmann to cause a shift to the left or shortening of the coagulation band, whereas fibrotic processes and those conditions associated with parenchymal damage of the liver cause a lengthening of the coagulation band or a shift to the right. In certain instances such as tuberculosis, exudation and fibrosis may occur together and then the coagulation band may be normal, or reflect the predominant process. Hepatic damage may occur together with a severe exudative process such as is sometimes seen in lobar pneumonia, and in such cases the shift to the left which occurs as a result of the pneumonia may be partially offset by the liver damage which by itself would produce a shift to the right.

Although there have been many publications concerning the Weltmann reaction, all but one have been in the non-English foreign literature. Kraemer's [2] report was the first in this country, but he concerned himself only with the use of the Weltmann reaction in diseases of the liver. Foreign workers, particularly those in Germany, are enthusiastic about the possibilities of the test as a diagnostic and prognostic aid.

We have studied the Weltmann reaction in over 2,000 cases of various diseases and have simultaneously compared it with the sedimentation rate in a number of instances. In some conditions, especially tuberculosis, acute rheumatic fever and lobar pneumonia, the coagulation band and the sedimentation rate were repeatedly determined in the same individuals over long periods of time.

Material Studied

Our material consists of patients admitted to the Cook County Hospital, the Research and Educational Hospital, and some seen in private practice. If a definite diagnosis could not be made either clinically or at autopsy, the case was discarded from our series. Weltmann's original technic was used for determining the coagulation band, and the sedimentation rate was determined by the method of Wintrobe and Landsberg.[3] At the beginning of the work Linzenmeier's [4] method was used, but it soon became evident that for accurate comparisons, corrections should be made for anemia. This was especially true for cases of tuberculosis and sepsis. Also in some con-

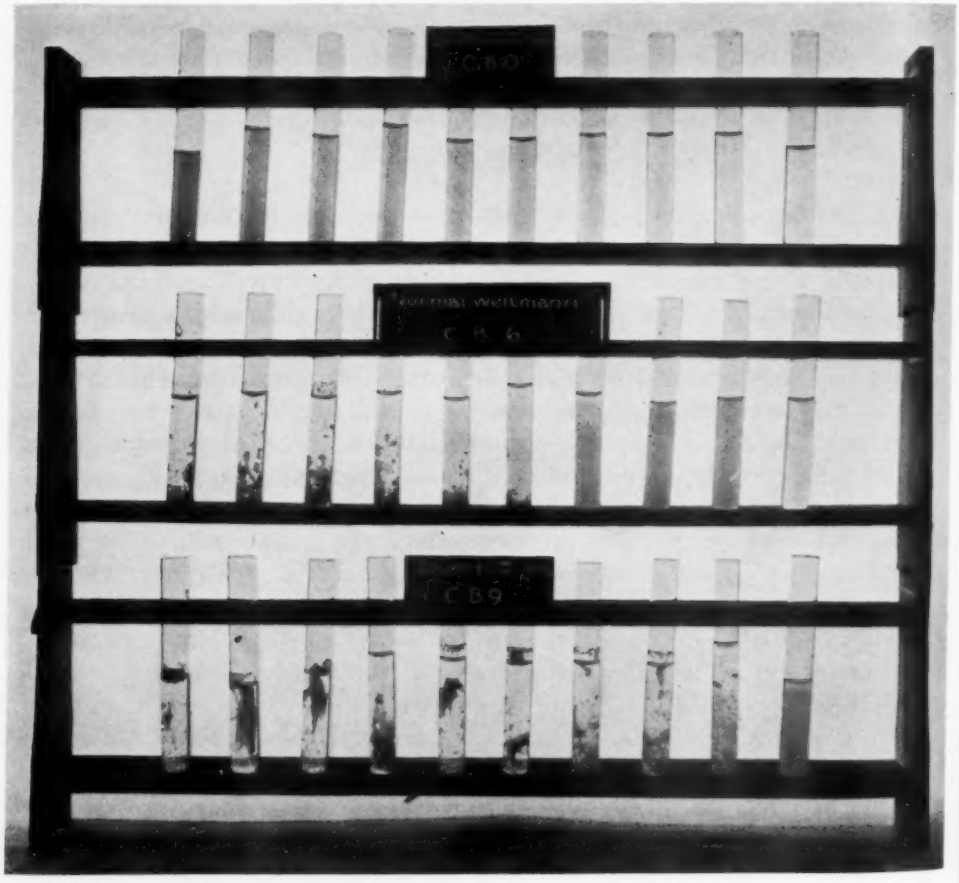

Fig. 1. A photograph illustrating the three different zones in the Weltmann reaction.[5]

The top row shows no coagulation in any of the tubes, indicating a marked shift to the left. The coagulation band is zero. This is from a patient with lobar pneumonia.

The middle row shows a normal Weltmann reaction with coagulation extending to the sixth tube and giving a coagulation band of 6.

The bottom row shows coagulation to the ninth tube, illustrating a marked shift to the right with a coagulation band of 9. This is from a patient with cirrhosis of the liver.

ditions like pneumonia and dysentery the concentrations of the blood varied greatly from day to day, being affected in a great measure by the intravenous administration of fluids, so that when the sedimentation rate was not corrected, erroneous results were obtained.

In figure 1 we reproduce an illustration which appeared in an earlier report of ours.[5] The ease with which the test can be read is apparent.

In figure 2 we have grouped according to the coagulation band a large

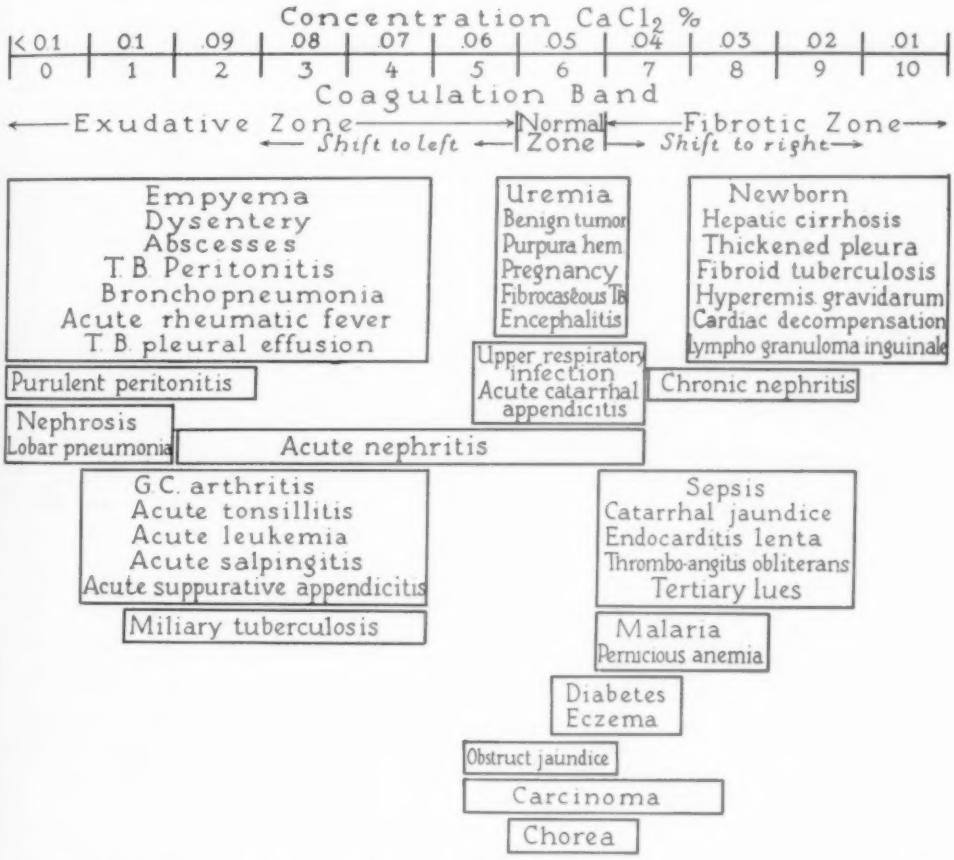

FIG. 2. A chart illustrating the three zones of the Weltmann reaction. The ranges of the coagulation band in some of the diseases studied are shown.

number of the conditions that were studied. A similar table on a much smaller scale was presented by Purper.[6] It is seen that the acute exudative diseases give a low coagulation band or shift to the left in the Weltmann reaction. The degree of the shift to the left is usually proportional to the magnitude of the exudative process. Lobar pneumonia and acute suppurative appendicitis, for example, give a greater shift to the left than bronchopneumonia or acute catarrhal appendicitis. Febrile conditions un-

associated with foci of inflammation, or in which the latter play a very minor rôle, usually give an increased coagulation band. Malaria, septicemia and endocarditis lenta are examples of this. Predominantly fibrotic conditions such as hepatic cirrhosis, fibrous tuberculosis, thrombo-angiitis obliterans and tertiary lues also give a shift to the right. The same is true for catarrhal jaundice, whereas obstructive jaundice usually gives a normal Weltmann reaction. Among the conditions which give a normal coagulation band are uremia, diabetes, pregnancy, encephalitis and tumors.

The only non-febrile, non-inflammatory condition which has, in our experience, given a marked shift to the left is the nephrotic syndrome. The coagulation band here is usually zero, even though the patient has lost his edema and is clinically improved. The shift to the left does not primarily depend upon the serum protein changes since it persists even when the blood chemistry approaches normal levels.

The Weltmann reaction is of practical value in the differential diagnosis of febrile disturbances because it establishes the nature of the pathological condition, that is, whether it is an exudative or a non-exudative or septic state. To illustrate, we present the following two case reports.

The Weltmann Reaction in a Patient with Typhoid Fever

Case 1. L. C., a colored boy of 9, was admitted to the Cook County Hospital on July 18, 1936, with the complaints of abdominal pain for four days, and nausea, vomiting and fever for two days. He had been perfectly well up to July 15 when he began to have cramp-like pain in the abdomen, especially on the right side. Two days later he became nauseated and began to vomit everything he ate, and fever was noted for the first time. He felt better the following day, but that evening he began to cough, his abdomen seemed to be "swollen" and he was delirious. On admission to the hospital his temperature was 104° F., pulse 120, respirations 28. The abdomen was distended and moderately tender, especially in the right lower quadrant, but there was no definite rebound rigidity. Peristaltic sounds were slightly less than normal. There were a few coarse râles in both pulmonary bases but physical examination otherwise was negative. The white blood count was 12,000 with 70 per cent polymorphonuclear leukocytes. The provisional diagnosis was peritonitis due to a ruptured appendix or pneumonia. Careful examination the next day did not reveal evidence which would warrant a diagnosis of peritonitis, and the patient was transferred to the medical service.

On July 20 the Weltmann reaction gave a coagulation band of 6, which was interpreted as ruling out an acute exudative condition like pneumonia or purulent peritonitis, and being in favor of a septic infection or typhoid fever, and a blood culture was suggested. Roentgenogram of the chest made the following day showed no abnormality. The blood culture taken July 22 was positive for *B. typhosus* and on July 24 the same organism was isolated from the stool. Although he was quite toxic and his temperature remained about 105° F. for 10 days, the boy became afebrile after three weeks and made an uneventful recovery. The coagulation band was determined five times during the boy's illness and at no time was there a shift to the left.

The Weltmann Reaction in a Patient with Endocarditis Lenta

Case 2. A. R., a white boy 6 years old, was admitted to the Cook County Hospital January 29, 1937 complaining of pains in the legs, which began two weeks

previously and lasted for about six days. He had been in bed since the onset, perspired easily, and seemed warm. Three days before admission he complained of pain in the right side of the abdomen, and he vomited four times. The day before entrance into the hospital he had a severe nosebleed. The past history and family history were negative except that one brother had rheumatic heart disease.

On admission the rectal temperature was 99° F., pulse 100 and respirations 24. Physical examination revealed a pale, under-developed boy of 6 who seemed alert and had no special complaints. There was dried blood in the right nostril, the tonsils were large, cryptic and slightly reddened, and there were several carious teeth. The left heart border was out to the anterior axillary line, and the right border 1 cm. beyond the right sternal margin. There was a long loud systolic murmur at the apex. The heart tones were loud and regular. The abdomen and extremities were negative.

The white blood count was 15,400 with 89 per cent polymorphonuclear leukocytes, and the red blood count was 3,250,000 with 46 per cent hemoglobin. The urine showed a trace of albumin. A two meter roentgenogram of the heart showed moderate cardiac enlargement of the mitral type. The electrocardiogram was essentially normal.

The provisional diagnosis was an acute exacerbation of chronic rheumatic carditis with mitral insufficiency. The following day the temperature rose to 102° F., the sedimentation rate was 30 mm. and the coagulation band 5. The patient continued to be febrile and two days later the coagulation band was again 5 and on February 10, eleven days after admission, it was 6. The normal coagulation band was at variance with our findings of a marked shift to the left in cases of active rheumatic carditis. Although there were no petechiae and the spleen at this time was not palpable, a diagnosis of subacute bacterial endocarditis was made. The next day the spleen became palpable and petechiae appeared a week later. Although early blood cultures were negative, in one obtained March 3 non-hemolytic streptococci were found and the formol gel test became positive. The septic course continued, and three blood transfusions were given, but the boy died 41 days after hospitalization. No autopsy was performed, although the diagnosis of subacute bacterial endocarditis was justified by the ultimate clinical course. In this case the Weltmann reaction spoke against acute rheumatic fever before the usual characteristics of subacute bacterial endocarditis appeared.

When considered with other laboratory findings the Weltmann reaction may help to make the diagnosis or may substantiate a diagnosis made previously. As more clinical conditions will be studied, the diagnostic possibilities of the test will doubtless be increased.

The Sedimentation Rate as a Diagnostic Aid

Of all non-specific laboratory tests, none has attracted more attention or been more widely acclaimed than the sedimentation rate of the erythrocytes. This test has been studied in practically all disease conditions, but its value is not agreed upon by various investigators. Inflammatory states and conditions associated with tissue destruction give a rapid sedimentation rate. A slow sedimentation rate has been characteristic only in allergic conditions and in the new born infant. The sedimentation rate has been of greatest value in detecting pathological conditions which are subclinical, and in following the progress of the individual in chronic conditions, especially tuberculosis and rheumatic fever. In the diagnosis of acute febrile

disturbances, the sedimentation rate is of little value since it is increased in almost all such conditions. Recently, however, it has been pointed out that in acute appendicitis the sedimentation rate is relatively normal, whereas in acute salpingitis it is increased.

Comparison of the Weltmann Reaction with the Sedimentation Rate

We have compared the coagulation band with the corrected sedimentation rate in 121 unselected cases as shown in figure 3. Our findings agree with those of Carrière, Martin and Duffossé,[7] in that there is no definite correlation between the Weltmann reaction and the sedimentation rate. Although a low coagulation band is very frequently associated with a rapid sedimentation rate, a normal or increased coagulation band may also be found with a rapid sedimentation rate. In those conditions which give a normal or increased coagulation band the sedimentation rate may be normal or rapid. A coagulation band of 6 or more with a rapid sedimentation rate may be found in malaria, sepsis, lymphogranuloma inguinale, tertiary syphilis and in the convalescent or healing stages of tuberculosis and rheumatic carditis.

Although the mechanisms of both the Weltmann reaction and the sedimentation rate are not known, the former depends on fewer factors and is more stable. In normal pregnancy the sedimentation rate is increased but the coagulation band is normal. It has also been shown [8] that there is a normal diurnal variation in the sedimentation rate which may be of such magnitude that in the same patient at one time of the day a normal value may be obtained, and at another time a pathological sedimentation rate may be found. This is not true of the Weltmann reaction. Yardumian,[9] after studying the influence of various factors on the sedimentation rate in over 2,000 conditions, concludes that "it is inconceivable that a phenomenon so readily influenced by many variable factors should be of appreciable diagnostic and prognostic value."

We have compared the sedimentation rate and coagulation band with the progress of the clinical condition in a large number of cases of lobar pneumonia, tuberculosis and rheumatic fever. In uncomplicated lobar pneumonia, the coagulation band gives a shift to the left, and in our experience has always been zero at the time of consolidation. After the onset of clinical resolution, the coagulation band begins to increase but takes several days to two weeks to return to normal. In those cases having more than one lobe of a lung involved, the coagulation band returns to normal more slowly than in those with only one lobe, or a portion of a lobe consolidated. The sedimentation rate is usually rapid at the onset of the condition, and is frequently still faster than normal when the coagulation band has returned to 6. We have constructed sedimentation curves, reading the sedimentation at 15 minute intervals for 1½ hours in a number of cases of lobar pneumonia

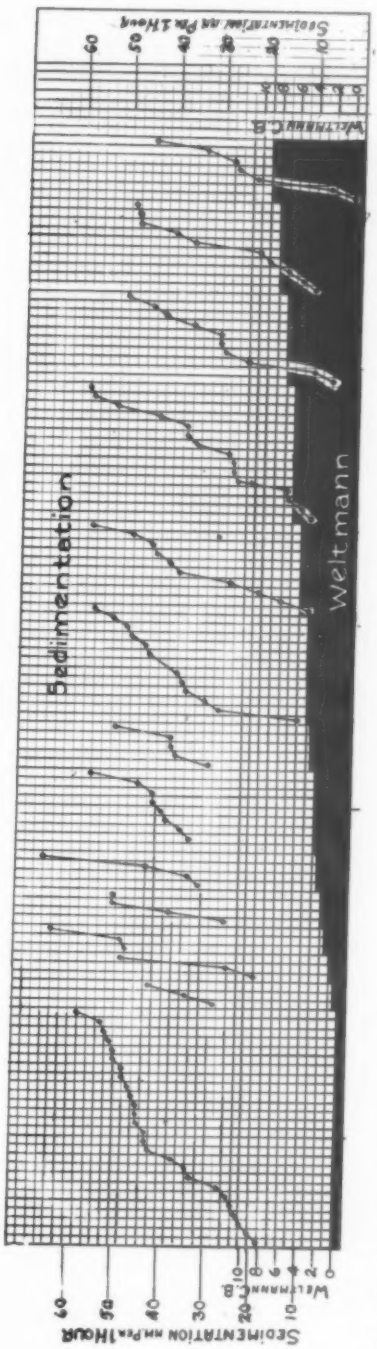

FIG. 3. A comparison between the coagulation band, indicated by the black area, and the corrected sedimentation rate, indicated by the connected dots. It is seen that a rapid sedimentation rate is found throughout the range of the coagulation band.

and cannot support the findings of Brooks [10] who stated that the sedimentation curves follow particular patterns according to the stage of the pneumonia. At the time of the crisis the sedimentation rate, in our hands, not infrequently becomes slower or even normal, and several days later returns to its former high level. Furthermore there is a great variation in the sedimentation rate from day to day irrespective of the clinical condition of the patient. This is especially true in children. We have illustrated these findings in the following figures.

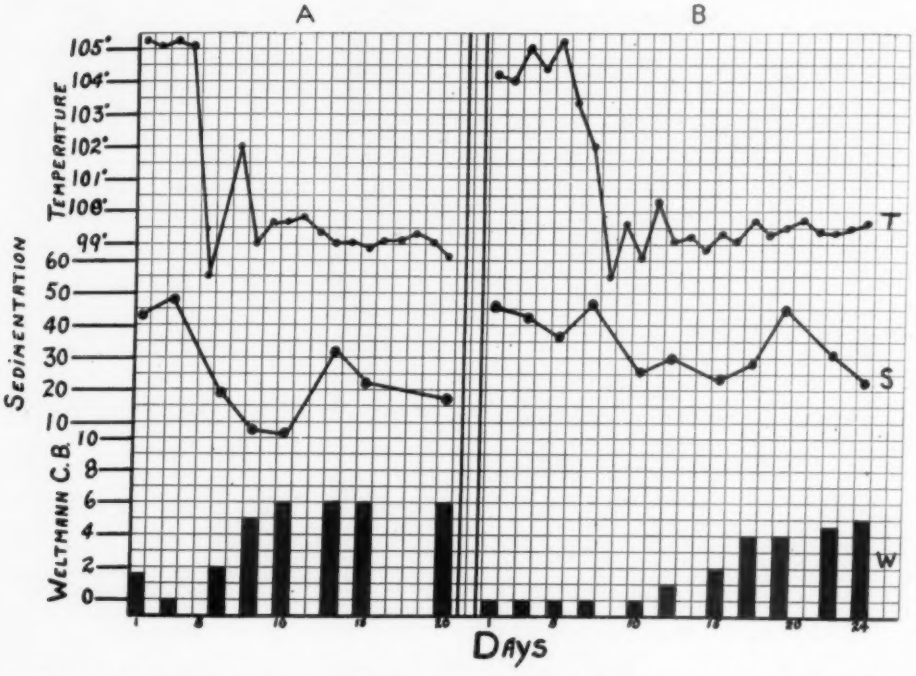

FIG. 4 *A*. Comparison of coagulation band, sedimentation rate and temperature in a case of lobar pneumonia with a consolidation of part of the right lower lobe.

B. Comparison of coagulation band, sedimentation rate and temperature in a case of lobar pneumonia with consolidation of the right middle and lower lobes.

DETAILED ANALYSIS OF PATIENTS WITH PNEUMONIA (FIGURE 4 A AND B)

C. R. (figure 4 A), a 6 year old Mexican boy, was admitted to the hospital December 28, 1936, with the complaints of cough for five days and pain in the chest, fever and rapid breathing for three days. On admission the temperature was 105.4° F., pulse 142 and respirations 40. There was clinical and fluoroscopic evidence of a pneumonia involving part of the right lower lobe. The white blood count was 20,000 with 86 per cent polymorphonuclear leukocytes. The clinical course was uneventful. There was a pseudo-crisis on the fourth hospital day (ninth day of illness) and the temperature was normal on the sixth day. On admission the coagulation band was 1½ and two days later it went down to zero. After resolution the coagula-

tion band returned rapidly to normal and reached 6 on the third afebrile day. The sedimentation rate was rapid at the beginning of observation, dropped to normal during the crisis and then rose again.

We compare this with another case of lobar pneumonia in which there was more extensive lung involvement.

L. A (figure 4 B), a white boy of 7, was admitted to the hospital with complaints of cough for two weeks and fever and vomiting for one day. On admission his temperature was 104.6° F., pulse 138 and respirations 42. There were signs of consolidation in the right middle and lower pulmonary lobes. The white blood count was 33,000 with 79 per cent polymorphonuclear leukocytes. The first coagulation band was determined on the sixth hospital day (seventh day of illness) and was zero. The sedimentation rate was 45 mm. in one hour. The boy was very toxic but had a crisis on the eighth day of observation or fifteenth day of illness and went home 16 days after the crisis. The coagulation band began to increase on the fourth afebrile day but was 5 (slightly to the left) on the sixteenth day when he went home. The sedimentation rate fluctuated considerably, showed a distinct drop after the crisis, and then rose to its former high level 11 days after the crisis.

Detailed Analysis of Patient with Empyema (Figure 5)

A. R., a boy of 13, was admitted to the hospital complaining of pain in the left chest, fever and severe abdominal pain for two days. The clinical findings were those of a left lower lobar pneumonia. Temperature was 102° F., pulse 120, respirations 26. The following day a roentgenogram showed a small amount of clouding in the lower left lung field. An empyema was detected on the fifth day and after the chest had been tapped several times, closed drainage was instituted on the eleventh day. The boy was very sick and toxic for two weeks, but he gradually improved and went home after having been in the hospital 77 days. At the time of discharge there was only slight drainage.

In figure 5 the Weltmann reaction is compared with the sedimentation rate and temperature. Throughout the 77 days the sedimentation rate remained rapid at about the same level, and thus did not at all reflect the clinical progress of the patient. The

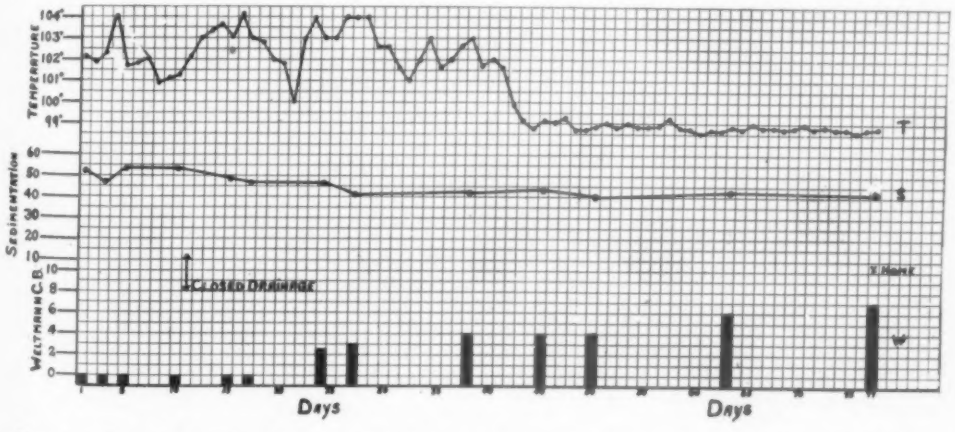

Fig. 5. Chart comparing the coagulation band, sedimentation rate, and temperature in a 13 year old boy with pneumonia and empyema.

coagulation band, however, was zero at the onset of observation and began to increase after adequate drainage was begun and became normal on the sixty-third day. In this case the coagulation band was a much better index of the clinical and pathological events than the sedimentation rate.

Comparison of the Weltmann Reaction with the Sedimentation Rate in Acute Rheumatic Fever

Numerous investigators [11] have stressed the value of the sedimentation rate as a guide in determining activity of the rheumatic process. We have studied and compared the sedimentation rate and the coagulation band in more than 100 cases of acute rheumatic fever of childhood, and our observations on the sedimentation rate agree with the reports previously mentioned. Simple chorea unassociated with carditis gives a normal sedimentation rate, irrespective of the clinical severity of the condition. Acute rheumatic arthritis and carditis give rapid sedimentation rates. After the disappearance of the clinical signs and symptoms of infection, the sedimentation rate remains rapid for variable lengths of time. In monocyclic rheumatic arthritis, the average time required for the sedimentation rate to return to normal after the patient was free from fever was three weeks. In polycyclic rheumatic arthritis, the sedimentation rate remained faster than normal for two months, whereas in carditis it was often three to five months before the sedimentation rate became normal.

The coagulation band in chorea is usually normal, but in acute rheumatic arthritis and carditis there is a shift to the left which is in most cases proportional to the severity of the clinical condition. The sedimentation rate, however, is just as rapid in a mild case as in a severe case. As improvement occurs the coagulation band returns to normal before the sedimentation rate, and frequently even shows a shift to the right when the sedimentation rate is still rapid.

Although the sedimentation rate must still be regarded as the best available criterion as to when the patient with acute rheumatic fever may be allowed to resume a more active life, we do not believe that the rheumatic infection remains active in all cases as long as the sedimentation rate is rapid. When the clinical condition of the patient indicates subsidence of the infection and the coagulation band has returned to normal, the patient is convalescing even though the sedimentation rate may be as rapid as when there was fever, tachycardia and joint pains. The sedimentation rate cannot be used as an index of the onset of convalescence or repair because it frequently is just as rapid when fibrosis is taking place as when there is an acute inflammatory exudative process. We have shown this in an example of empyema (figure 5). When the sedimentation rate becomes normal and convalescence is over, the whole train of pathological events has come to a standstill and the patient is restored to normal. From this viewpoint the sedimentation rate is a better guide in determining when the rheumatic process is ended, but the coagulation band gives a truer insight into the actual pathological events taking place.

Discussion

Our results in the main agree with most of the published reports in the European literature on the Weltmann sero-coagulation band. The Weltmann reaction is a simple and easy test which distinguishes exudative from productive anatomic changes, and therefore becomes a valuable diagnostic criterion as well as a prognostic aid in various disease conditions. Examples of this we have presented in the text.

In view of the fact that this test is a nonspecific reaction and is not diagnostic of any disease, the clinician must interpret the Weltmann coagulation band as another biological reaction which the patient presents and evaluate it accordingly. When the laboratory worker examines the patient's serum he can only state that the reaction is in the normal zone, gives a shift to the left in the exudative zone or to the right in the fibrotic or septic zone. The clinician familiar with the patient's clinical history and physical findings can now interpret the Weltmann reaction in a fashion which will enable him to at once classify the patient's condition as one of exudative or fibrotic anatomic changes. For example, in pulmonary tuberculosis exudative changes result in a coagulation band to the left, whereas fibrotic changes give a coagulation band to the right.

When we apply the Weltmann reaction to a great variety of clinical conditions we obtain valuable assistance from this test particularly in relation to diagnosis. It is fairly well established that the normal coagulation band is in tube 6 to 6½, representing the concentration of $CaCl_2$ in 0.05 per cent to 0.04 per cent. We shall now briefly indicate the diagnostic value of the Weltmann reaction in some of the more important diseases, and have arranged these for the sake of simplicity, according to systems.

The Weltmann Reaction as a Diagnostic Aid in Some of the More Important Diseases

Liver Diseases. As a rule in diseases of the liver and gall-bladder, the coagulation band is shifted to the right, more markedly so if there is cirrhosis or a parenchymatous affection of the liver. In obstructive jaundice, due either to stone or neoplasm, the coagulation band is within normal limits. In hepatic diseases associated with jaundice or ascites, the coagulation band is not materially affected as far as a swing to the right is concerned. Thus, in catarrhal jaundice when there is a disturbance in the parenchyma of the liver, the coagulation band extends to tubes 7 and 8; and when there is atrophy of the liver as in cirrhosis of the liver, the coagulation band extends to the ninth or the tenth tube.

We had an opportunity to examine the Weltmann reaction in salvarsan icterus and we have observed that the coagulation band usually reaches the eighth or ninth tube. Weltmann and Sieder [12] have pointed out that icterus due to antimony gave a similar result.

Infections. In various septic conditions and frequently in typhoid fever, the coagulation band reaches tubes 6 to 8. It is this important manifestation that differentiates sepsis from pneumonia, abscess, gangrene and other exudative lesions. Purper [13] has also indicated that the Weltmann reaction can be used as a differential diagnostic test in separating sepsis from the various forms of exudative changes. In most cases of typhoid fever we have obtained a normal coagulation band in the different weeks of the disease. Kretz and Kudlac [14] and Scherleitner [15] have obtained a shortened coagulation band in the first week of typhoid fever, but as a rule the Weltmann reaction in our cases was within normal limits. This reaction is altered when complications such as pneumonia, perforation and peritonitis occur, and then the coagulation band swings toward the left.

In scarlet fever, particularly in the first week of the disease, the coagulation band may vary anywhere from zero to tube 4, although Kretz and Kudlac [14] in their series of scarlet fever patients examined between the first and sixth week of the disease reported a normal coagulation band.

Cardiovascular Diseases. Non-infective heart disease gives a normal coagulation band. This is true particularly if the cardiac condition is compensated. Should the disease process progress toward decompensation, then there is a tendency for the Weltmann reaction to shift toward the right, which reflects a parenchymal damage to the liver. Similar observations in heart disease were shown by Kisch.[16]

In acute rheumatic carditis the coagulation band ranges from zero to tube 5, and in subacute bacterial endocarditis from tube 5 to tube 9. This suggests the possibility of the Weltmann reaction as a diagnostic criterion in distinguishing these two types of heart disease.

Vascular Diseases. Thrombosis and occlusion of the blood vessels usually were accompanied by a normal coagulation band or a slight shift to the right. If this condition was associated with destructive changes in the surrounding tissues, or if the disease was accompanied by a cellulitis or a lymphadenitis, the coagulation band gave a marked shift to the left and at times reached the first tube.

Blood Dyscrasias. The acute leukemias gave a shift to the left whereas the chronic leukemias usually gave a normal or increased coagulation band. In those diseases of the blood associated with fibrosis of the spleen such as Hodgkin's disease, Cooley's anemia, Banti's disease and sickle cell anemia, the coagulation band was also increased, whereas in the simple secondary anemias and in purpura hemorrhagica it was normal.

Bone. In arthritis, the Weltmann reaction was within the normal zone or gave a slight shift to the right. Hennes and Kemen [17] observed 38 cases of primary chronic polyarthritis of which 26 were proliferative and 12 exudative in nature. The authors compared the coagulation band with the sedimentation rate and pointed out that there was no correlation between these two tests.

In acute rheumatic arthritis, osteomyelitis and gonococcal arthritis, the

coagulation band was usually shortened in proportion to the severity of the condition. In chronic arthritis and quiescent gonorrheal arthritis the Weltmann reaction was within the normal zone. In early cases of gout the coagulation band was in tube 1. In acute osteo-arthritis of the ankles, hips and spine, the coagulation band gave a distinct shift to the left. In septic arthritis the Weltmann reaction was more nearly normal even though the joint was severely involved. The septic state usually overshadows the exudative process and draws the coagulation band toward the normal.

Pregnancy. The Weltmann reaction is within normal limits in pregnancy, but fetal blood as a rule gave a prolonged coagulation band which may be due to the physiological insufficiency of the liver in the new born. In the toxemias of pregnancy, the coagulation band showed a shift to the left.

In *gynecological conditions* particularly when the Fallopian tubes show inflammatory changes, the coagulation band is of great assistance in diagnosis. Here the coagulation band gives a shift to the left to tube 2, and in subacute salpingitis the coagulation band swings toward the right to tubes 4 and 5. As the pathological condition becomes quiescent the Weltmann reaction is normal or slightly to the right. In incomplete abortion, the coagulation band may vary from tube 3 to tube 6. In all benign tumors of the uterus the Weltmann reaction was normal or slightly to the right.

Gastrointestinal Diseases. Benign processes such as ulcers of the stomach or duodenum, during the quiescent stage, give a normal coagulation band. When complications such as perforation occur, the Weltmann reaction immediately shifts to the left. This also holds true when bleeding occurs in cases of peptic or duodenal ulcer. Terminal ileitis gives a Weltmann reaction in tube 6.

Appendicitis. The Weltmann reaction is of marked assistance in the diagnosis of exudative involvement of the appendix. We have had occasion to determine the coagulation band before operation in many patients in whom a clinical diagnosis of acute or chronic appendicitis had been made. Invariably if the coagulation band gave a shift to the left, the gross as well as the histological examination of the appendix removed revealed either acute suppuration, gangrene, or peri-appendiceal abscess. In chronic appendicitis, fecoliths of the appendix, in fibrous obliterative appendicitis and in acute catarrhal appendicitis the coagulation band was normal.

Kidneys. Most renal conditions are secondary to or associated with pathological conditions elsewhere in the body so that there is a wide variation in the coagulation band. Acute nephritis may give a shift to the left, a normal coagulation band or even a slight shift to the right. In post-scarlatinal nephritis the coagulation band may be wider than in nephritis associated more directly with foci of inflammation such as tonsillitis or cervical adenitis. Chronic nephritis gives a marked shift to the right, but in the nephrotic syndrome the coagulation band is very low, being zero in most

cases. Pyelitis gives a variable reaction similar to that found in acute nephritis, but perinephritic abscess gives a constant shift to the left. In cases of uremia without inflammatory complications the coagulation band is usually normal. The same is true for hydronephrosis.

Skin. In lymphogranuloma inguinale the coagulation band varies according to the condition of the lesions. When there is much tissue destruction the coagulation band is narrow, and when fibrosis is the predominant process it is far to the right, being often 9 or 10. The sedimentation rate is usually rapid irrespective of the coagulation band. Chancroids and chancres give a normal reaction, or one slightly below normal in tube 5. Secondary or tertiary syphilis usually will cause the coagulation band to deviate toward the right. This apparently reflects productive changes which are the rule in syphilis, and is in contrast with exudative changes which may occur in tuberculosis. It is of interest to note here that the shift to the right in syphilis is independent of the positive or negative Wassermann reaction.

Diabetes. In our series of patients who had diabetes mellitus the coagulation band was normal or slightly above normal. When complications occur such as gangrene or vascular occlusion, the coagulation band may drop to normal or slightly below normal.

Tumors. In benign tumors of all types the Weltmann reaction invariably was within the normal zone. In carcinoma, as a rule, the Weltmann reaction gave a slight shift to the left, and as the carcinoma underwent degenerative changes to the stage of necrosis and abscess formation, the Weltmann reaction gave a shift to the left, and at times to the zero or first tube. When metastases occurred the Weltmann reaction shifted to the left.

Miscellaneous. Froelich's syndrome gives a coagulation band in tube 8. In myxedema, the coagulation band was 5; and in Paget's disease the coagulation band was in tube 8. In hemorrhage and trauma of the brain which did not result in an immediate death the Weltmann reaction, as a rule, was either normal or slightly below normal in tube 5. In purulent infections of the brain and all suppurative forms of meningitis the Weltmann reaction was invariably in tube zero. In encephalitis and in lead encephalopathy the coagulation band was usually normal. Tuberculous meningitis gives a moderate shift to the left. In hypo- and hyperthyroidism the coagulation band was in tubes 5 to 7.

Spinal fluid invariably gives a negative reaction in tube zero, obviously due to the extremely low total protein. We have had occasion to examine blood and ascitic fluid from a patient with cirrhosis of the liver. The coagulation band in ascitic fluid was in one tube less than the coagulation band of the blood. For example, when the coagulation band was in tube 7 the ascitic fluid was in tube 6, and when the coagulation band of the blood was in tube 6 the ascitic fluid was in tube 5.

The Weltmann Reaction as an Aid in Prognosis

From the standpoint of prognosis the Weltmann sero-coagulation band is extremely helpful. This is particularly true when the Weltmann reaction is repeated frequently in the same patient. This test reflects anatomic alterations so that when the coagulation band shifts to the left it manifests exudative changes, and as it swings toward the right it indicates fibrotic processes. This reaction suggests that the clinical condition is either becoming unfavorable and that complications have developed as is manifested by the coagulation band in the exudative zone, or that the pathological condition is becoming arrested and that the patient is improving as indicated by a return to normal or to the fibrotic zone. The sedimentation reaction has been used extensively in prognosis as well as an aid in the differential diagnosis of various clinical conditions. We have compared this test with the Weltmann reaction and have found that the coagulation band does not at all times agree with the sedimentation reaction. In fact the sedimentation reaction has at times been misleading in interpreting the patient's clinical progress. For example, in both rheumatic carditis and endocarditis lenta, the sedimentation reaction is rapid although in the former condition the underlying anatomic change is exudative, and in the latter septic. The Weltmann reaction here is of more assistance, since in rheumatic carditis it gives a shift to the left and approaches normal as the process becomes arrested; whereas, in endocarditis lenta, the coagulation band is normal or to the right. Another example of the divergence of interpretation between the sedimentation and the Weltmann reactions is that of sepsis. In this condition the Weltmann reaction gives a normal coagulation band or a shift to the right whereas the sedimentation reaction is rapid. The coagulation band may also be used in prognosis as a quantitative index of tissue destruction and repair, as is seen in tuberculosis.

Mechanism of the Weltmann Reaction

As to the mechanism of the Weltmann reaction very little is known. Nannini and Marani [18] believed that an increase in the globulin and a decrease in the albumin is necessary for a shortening of the coagulation band. In contrast to this Carrière, Martin and Duffossé [7] could find no relation between the coagulation band and the albumin-globulin ratio.

In 75 patients the Weltmann reaction was compared with the total serum protein, albumin, globulin and the albumin-globulin ratio.

Table 1a illustrates the total serum protein values as compared with the coagulation band. It is seen that where the total serum protein is less than 7 mg. per cent the coagulation band may extend throughout the range from 0 to 9. Where the total serum protein is more than 7 mg. per cent the coagulation band is rarely less than normal. Table 1b compares the albumin-globulin ratio with the coagulation band. Where the albumin-globulin ratio is less than 1.5 the Weltmann reaction may be normal or give

TABLE IA

Relation of Total Serum Protein to Coagulation Band

No. Cases	Total Protein		Range of Coagulation Band										
			0	1	2	3	4	5	6	7	8	9	10
22	−5 mg.	Case	5	2	3	1	2	5	2	1	0	1	0
41	5–7 mg.	Distrib.	1	2	3	3	3	7	13	3	6	1	0
12	+7 mg.		0	0	0	0	2	0	5	1	2	2	0

TABLE IB

Relation of A/G Ratio to Coagulation Band

No. Cases	A/G Ratio		Range of Coagulation Band										
			0	1	2	3	4	5	6	7	8	9	10
27	−1	Case	3	2	3	0	2	4	3	2	6	2	0
30	1–1.5	Distrib.	3	2	1	4	4	5	5	3	2	1	0
13	1.5–2.0	"	0	0	0	0	0	2	7	3	1	0	0
5	+2.0		0	0	1	0	1	0	2	0	0	1	0

either a shift to the left or right. Where the albumin-globulin ratio is more than 1.5 the coagulation band is more apt to be normal or greater than normal. We may conclude that the coagulation band gives no index as to the total serum protein or the albumin-globulin ratio. That the albumin-globulin ratio by itself is of little importance is further seen in table 2. In the nephrotic syndrome the total serum protein and the albumin are low, the globulin is normal or slightly increased, and there is an inverted albumin-globulin ratio. In this condition the coagulation band is to the left in the

TABLE II

	Total proteins	Albumin	Globulin	Albumin-globulin ratio	Weltmann
Nephrotic syndrome.....	3.58	1.33	2.25	0.59	0
Nephrotic syndrome.....	4.50	1.50	3.00	0.50	1
Cirrhosis of liver with ascites..	4.10	1.10	3.00	0.36	7
Cirrhosis of liver with ascites..	4.90	1.50	3.40	0.44	7

exudative zone in tube zero or tube 1. This is contrasted with an example of cirrhosis of the liver with ascites in which the quantitative protein picture of the serum is identical with that of nephrosis but here a normal or increased coagulation band is obtained in tube 7.

Goettsch and Reeves [19] believe that the serum proteins in nephrosis differ immunologically from normal serum proteins and this change may therefore be a significant factor.

Other suggestions as to the probable mechanism of the Weltmann reaction have been made by several investigators, but no definite proof has been given. Kretz and Kudlac [14] found that the chloride and calcium content of the serum have no effect on the coagulation band. They believe that the reaction depends upon a qualitative change in the serum protein. Weltmann found that the addition of bile does not alter the reaction. Hemolysis will cause an increased coagulation band.

The chemistry of the changes occurring in heat coagulation of protein are not completely understood, but several factors play a rôle. The most important appear to be the nature and amount of the protein itself, the pH, and the electrolytic content of the surrounding medium. Each protein itself may have its optimum pH and electrolytic threshold. Just what rôle is played by the electrolyte is difficult to estimate. We have determined the pH of the various dilutions of $CaCl_2$ used in the reaction and found that the range of the pH was between 7.5 and 7.73 and it had no appreciable effect on the coagulation band. However, we have correlated the blood pH with the coagulation band and found that at times when there was a decrease of the pH of the serum there was a tendency for the coagulation band to become increased, and conversely, when the pH of the serum approached the alkaline side the coagulation band was decreased. This became more prominent when the blood pH was repeated often on the same patient, and we reported this in a previous publication.[20] We do not believe, however, that there is any essential relationship between the pH and the coagulation band. Both may be manifestations of the same underlying process. Some investigators as di Benedetto and Stornello [21] have pointed out that the reticulo-endothelial system is concerned with the management of the physical chemical equilibrium of the blood serum, which in different degrees of intensity may be common to several diseases.

We have performed in vitro absorption experiments using the method of Hektoen and Welker [22] in an attempt to obtain, if possible, some information as to the specificity of the negative phase in precipitin production.* Under the conditions of our experiment the serum obtained from a patient showing a coagulation band in tube zero, did not appear to contain antigenic protein material which was not also present in normal serum showing a coagulation band in tube 6. In other words the precipitin reaction of the blood from a patient with a zero coagulation band, one from a normal coagulation band, and one with a coagulation band in tube 9, all gave precipitin reactions within the normal range.

Conclusions

The Weltmann serum coagulation reaction is a simple test, easy to perform, and can be read within 15 to 20 minutes. It can be performed in a hospital laboratory as well as in a doctor's office. The test is not diagnostic

* The immuno-chemical experiments were performed by Dr. C. A. Johnson of the Department of Physiological Chemistry of the University of Illinois College of Medicine.

for any disease, but is a nonspecific reaction which aids in distinguishing exudative from fibrotic processes. The normal coagulation band is between tubes 6 and 6½. When the coagulation band is limited to the first five tubes or less it indicates a shift to the left or an exudative reaction. When the coagulation band extends to more than six tubes, there is a shift to the right which indicates fibrotic changes. In general, acute inflammatory and exudative conditions cause a shortened coagulation band, whereas in chronic diseases characterized by predominating fibrotic processes, in healing stages of acute infections, in sepsis, and in parenchymatous liver damage, the coagulation band tends to be lengthened.

The coagulation band does not always agree with the sedimentation rate and reflects more accurately the pathologic-anatomic changes.

Although the mechanism of the serum coagulation reaction is not known, we believe that the Weltmann test may be a diagnostic as well as a prognostic aid in certain disease conditions, and has been shown to be of especial value in tuberculosis and rheumatic fever, and in distinguishing septic from non-septic febrile states.

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PATHOLOGIC FINDINGS IN THE HEART IN SUDDEN CARDIAC DEATHS*

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This communication is the report of a study of 41 hearts obtained from subjects who died suddenly from cardiac disease. One was from private practice † and 40 occurred at the New York City Hospital between January 1, 1927 and July 1, 1936.

During that period there were 82 cases of sudden death in the hospital that came to autopsy. Twenty-two were proved to be due to non-cardiac factors such as ruptured aneurysm, brain tumors, massive hemorrhage, etc. Of the remaining 60 cases 20 had to be discarded because of unsatisfactory histologic material.

For the purpose of this study cases were considered as sudden death when death was instantaneous or occurred within a few minutes after collapse. In none was it delayed more than 20 minutes and usually the time limit was less than ten.

Our findings proved to be different from the commonly accepted beliefs of the present day. We found the chief etiologic factor producing cardiac changes in these cases was infection, whereas arteriosclerosis occurred as a main factor in a comparatively small number.

Histopathologic Changes

The cases were classified for a working basis according to the main clinical or pathological diagnoses. The following table (1) gives the classification:

Table I

Acute coronary thrombosis	10
Acute endocarditis	5
Acute coronary insufficiency	5
Deaths in infancy and childhood	5
Rheumatic heart disease	4
Syphilis and essential hypertension	4
Acquired syphilis	2
Syphilis and rheumatic heart disease	2
Acute pneumonia	2
Unexplained deaths	2
Total	41

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† Thanks are due to Dr. George R. Irving, New York City, for permission to include this case.

The one common pathologic finding in the entire series, with the exception of the two deaths that were unexplainable, was a damage to the myocardial fibers. It varied in degree and extent in different instances. It was mildest in the cases with interstitial polynuclear reaction, such as was present in the acute pneumonias of the adult, in which there appeared a molecular degeneration of the cytoplasm and a disturbance of the finer architectural pattern of the fiber. It was most severe in instances of acute coronary thrombosis in which the myomalacia was visible to the naked eye. It was of interest to note that in the latter group histological changes of mild degree were found well beyond the region of infarction and frequently in the muscle supplied by vessels free of thrombi.

The etiology of the myocardial damage varied somewhat but the most striking finding was the rôle played by infection. In 14 cases of the entire series there was an infectious process directly affecting the heart. These consisted of four cases of acute rheumatic myocarditis, five cases of acute endocarditis, two cases of acquired syphilis, two cases of combined syphilis and hypertension with a superimposed acute infectious endocarditis and one case of acute coronary insufficiency with bacterial arteriolar thrombi. In several instances more than one infectious factor was present in the same heart. The findings in this group of infectious myocarditides are summarized in table 2.

The cardiac damage in 12 other cases seemed toxic rather than infectious in nature. In these there was acute infection in other organs but no demonstrable bacteria in the heart. In eight of this group the myocardial damage was characterized by marked molecular degeneration associated with polynuclear reaction. Of this group the two cases of acute pneumonia in adults are examples. This is not unusual as toxic changes of the myocardium are a well known accompaniment of pneumonia. The changes in these two instances seem to have progressed a step further, sufficient to initiate a cellular response. In one case definite infection of the heart may have been present since the pneumonia was complicated by mediastinitis and fibrinous pericarditis.

The two cases of rheumatic heart disease and syphilis also had acute pneumonia and cardiac lesions similar to those in the two cases just mentioned in the preceding paragraph. In one of these there may have been definite infection in addition to the acute toxic degeneration since there was a fibrinous pericarditis and peritonitis present.

One case of acute coronary insufficiency was similar. That the bronchopneumonia in this instance was not simply that seen so frequently as a terminal event in coronary arteriosclerosis is indicated by the clinical history. He had been compensated and ambulant under maintenance doses of digitalis for five months and was found dead in bed.

Three of the cases in infancy and childhood were of the same type. The clinical features of these cases had several points of interest. Two children were apparently convalescing from acute upper respiratory infections with

TABLE II

Infectious Myocarditides

Serial No.	Race	Sex	Age	Group	Under Observation	Anatomical Diagnoses	Remarks
1	W.	M.	18	R.H.D.	32 m	Chronic active rheumatic pancarditis. Acute rheumatic myocarditis. Acute bronchopneumonia. Acute fibrinous pericarditis.	Active rheumatic of moderate severity.
2	B.	M.	35	R.H.D.	4½ m	Chronic active rheumatic pancarditis. Acute rheumatic myocarditis.	Severe rheumatic without edema.
3	B.	F.	62	R.H.D.	1 m	Chronic active rheumatic valvulitis of mitral valve. Acute rheumatic myocarditis. Acute endocarditis of mitral valve. Acute myocardial abscesses.	Sarcoma uteri. Hysterectomy. Postoperative anginal attacks. Wound infection; streptococci in section.
4	W.	M.	41	R.H.D.	2 d	Healed rheumatic mitral valvulitis. Chronic active rheumatic valvulitis of tricuspid valve. Acute rheumatic myocarditis. Acute bronchopneumonia.	Paroxysmal dyspnea and cyanosis.
5	W.	M.	49	Acute endocard.	25 d	Chronic active rheumatic valvulitis of mitral aortic and pulmonic valves. Acute endocarditis of aortic valve. Acute myocardial abscesses. Acute splenic infarctions. Acute interstitial nephritis.	Slowly progressive congestive failure. Infected varicose ulcer of leg. No blood culture. Gram positive cocci in section of valve.
6	W.	M.	69	Acute endocard.	9 d	Healed rheumatic pancarditis. Acute endocarditis of mitral valve. Acute mural endocarditis of both ventricles. Acute arteriolar thrombi of LV and IVW. Acute miliary infarctions of heart.	Slowly progressive congestive failure. Joint pains. No blood culture.

TABLE II—*Continued*

Serial No.	Race	Sex	Age	Group	Under Observation	Anatomical Diagnoses	Remarks
7	W.	F.	28	Acute endocard.	20 d	Chronic active rheumatic valvulitis of mitral aortic and tricuspid valves. Acute gonococcal endocarditis of mitral and aortic valves. Acute gonococcal myocarditis. Emboli of spleen, kidneys and popliteal artery.	Clinically subacute bacterial endocarditis of 5 mos. duration. Positive blood cultures. Gonococci demonstrable in valves, myocardium and popliteal embolus.
8	B.	F.	21	Acute endocard.	23 d	Acute neisserian endocarditis of aortic valve with perforation through base of aorta into right auricle. Acute myocarditis.	3 wks. migrating arthritis following acute sore throat. Negative blood cultures. Organisms (meningococci?) in valve.
9	W.	M.	38	Acute endocard.	5 d	Acute staphylococcus endocarditis of tricuspid valve. Acute staphylococcus myocarditis. Acute staphylococcus abscess of prostate. Acute suppurative nephritis. Acute suppurative pericholecystitis. Chronic gonococcal prostatitis.	Urinary retention and instrumentation 1 mo. previously. Positive blood cultures *Staph. aur. hemo.* Staph. demonstrable in valve, myocardium and prostate; gonococci in prostate.
10	B.	M.	43	Acquired syphilis	11 m	Syphilis of aorta with incompetent valve and atresia of coronary mouths. Syphilitic myocarditis. Acute rheumatic myocarditis. Chronic pulmonary tuberculosis.	Ambulatory.
11	B.	F.	46	Acquired syphilis	20 d	Syphilis of aorta with incompetent valve and atresia of coronary mouths. Syphilitic myocarditis. Acute myocarditis (syphilitic?).	Decompensated.

TABLE II—*Continued*

Serial No.	Race	Sex	Age	Group	Under Observation	Anatomical Diagnoses	Remarks
15	B.	M.	42	Combined syphilis and hypertension	2 m	Commissural syphilis. Acute endocarditis of aortic valve. Syphilitic arteritis of intrinsic coronary arteries. Acute bronchopneumonia. Urethral strictures. Chronic pyelonephritis.	Congestive failure.
17	W.	M.	45	Combined syphilis and hypertension	3 m 1 m	Syphilis of aorta with incompetent valve. Acute endocarditis of aortic and mitral valves. Acute myocarditis. Arteriolar sclerosis of heart. Acute and subacute myocardial necroses. Acute bronchopneumonia. Chronic purulent bronchiectasis. Acute glomerulitis.	Clinically improving.
30	W.	M.	75	Acute coronary insufficiency	46 m	Acute miliary infarctions of heart. Bacterial arteriolar emboli of heart. Acute infarctions of kidneys. Chronic purulent bronchiectasis.	Partially decompensated.

FIG. 1. (Case 8.) Aortic valve in unidentified Neisserian endocarditis. The posterior leaflet is almost completely destroyed. The small diamond shaped defect toward the left in the sinus forms the base of a fungating mass presenting in the right auricle. The larger defect on the right is a deep ulcer filled with blood. The lesion of the leaflet is similar in Case 7.

a normal temperature for several days and evidence of gaining weight. The third child had apparently never been ill. He had been playing happily in his crib 15 minutes before being found dead. Another member of the family, however, had been confined to the home with acute sore throat, but was in isolation and had not been in contact with the child.

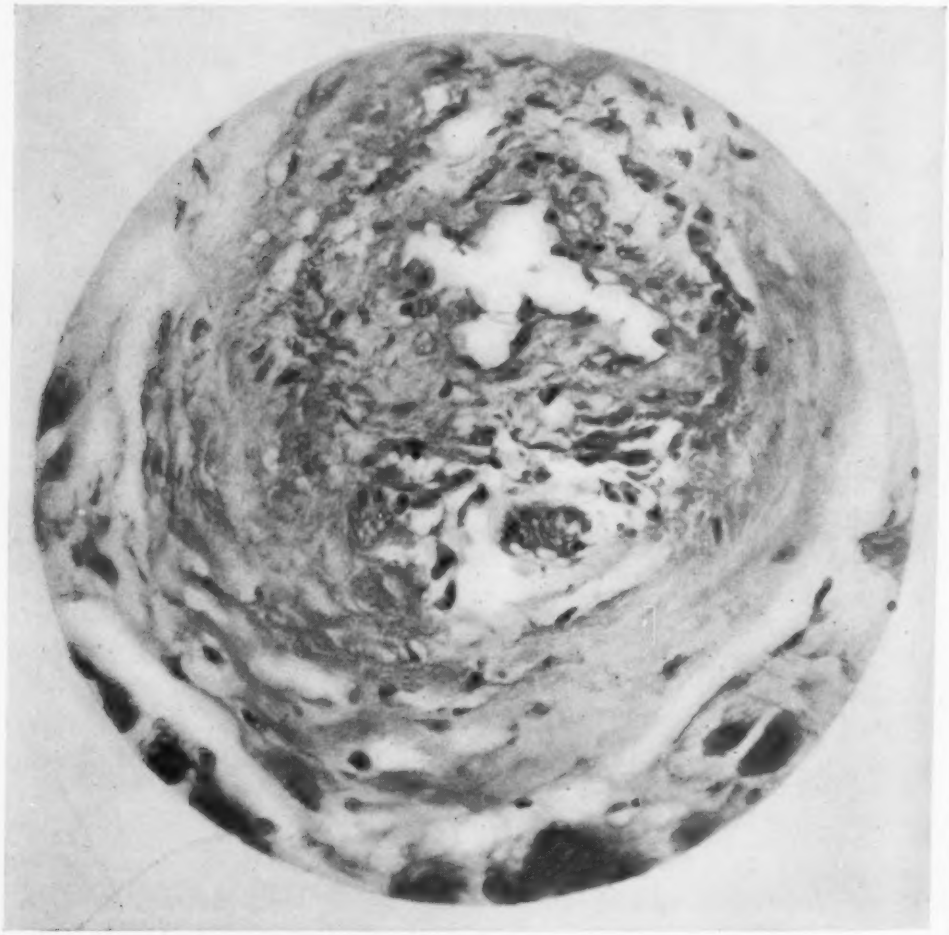

FIG. 2. (Case 15.) Syphilitic endarteritis of intrinsic coronary arteries in a case of combined syphilis and essential hypertension.

Two cases had acute coronary thrombosis of the superficial arteries and acute bronchopneumonia. One was in congestive failure. The other had suffered a first attack of angina a few days previously and clinically was improving rapidly. In this case the first attack had occurred a few days after a common head cold. The kidneys in both cases had focal glomerular lesions suggesting infection. Purulent masses were present in one, acute intracapillary hyaline thrombi in the other. In addition to the acute process,

TABLE III

Toxic Myocarditides

Serial No.	Race	Sex	Age	Group	Under Observation	Anatomical Diagnoses	Remarks
12	B.	M.	26	Combined syphilis and rheumatism	5 w	Chronic active rheumatic pancarditis. Acute rheumatic myocarditis (limited). Acute interstitial myocarditis. Acute fibrinous pericarditis. Syphilis of aorta with incompetent valve. Acute lobar pneumonia. Acute fibrinous peritonitis.	Congestive failure.
13	B.	M.	34	Combined syphilis and rheumatism	8 w 6½ m 9 d	Chronic active rheumatic valvulitis of mitral aortic and tricuspid valves. Acute rheumatic myocarditis (limited). Acute interstitial myocarditis. Commissural syphilis of aorta. Acute bronchopneumonia.	Decompensated; anginal attacks.
23	W.	M.	66	Acute coronary thrombosis	2 m	Recent coronary thrombosis. Chronic purulent bronchiectasis. Acute bronchopneumonia. Acute glomerulitis.	Decompensated.
26	W.	M.	59	Acute coronary thrombosis	2 d	Recent coronary thrombosis. Chronic purulent bronchiectasis. Acute bronchopneumonia. Acute glomerulitis.	Clinically improving.
28	B.	M.	60	Acute coronary insufficiency	6 m	Acute myocardial necrosis. Acute bronchopneumonia. Chronic purulent bronchiectasis.	Compensated 5 mos.

TABLE III—*Continued*

Serial No.	Race	Sex	Age	Group	Under Observation	Anatomical Diagnoses	Remarks
31	W.	M.	67	Acute coronary insufficiency	2 w	Acute medial necrosis of coronary artery. Acute myocardial necrosis. Chronic purulent bronchiectasis.	Very slight decompensation.
32	W.	M.	50	Acute coronary insufficiency	3 w	Acute medial necroses of coronary arteries. Acute myocardial necrosis. Chronic purulent bronchiectasis.	Compensated with limited reserve for 3 wks.
33	B.	M.	33	Acute pneumonia	5 d	Acute interstitial myocarditis. Acute lobar pneumonia. Acute mediastinitis. Acute fibrinous pericarditis. Sickle cell anemia.	
34	W.	F.	67	Acute pneumonia	1 d	Acute myocarditis. Acute bronchopneumonia.	
35	B.	F.	3 m	Infancy and childhood	23 d	Acute myocarditis. Acute bronchopneumonia.	Acute upper respiratory infection. Gastroenteritis. Recovery. Clinically well for 1 wk.
38	B.	F.	45 d	Infancy and childhood	45 d	Acute myocarditis. Acute streptococcal pneumonia. Acute streptococcal sinusitis.	Acute upper respiratory infection. Recovery. Clinically well for 1 wk. *Strept. viridans* in cultures of lungs and sinuses at autopsy.
39	W.	M.	4½ m	Infancy and childhood	—	Acute myocarditis. Acute streptococcal pneumonia. Status lymphaticus.	Never ill; found dead in crib. *Strept. viridans* in cultures of nasal discharge and lungs at autopsy.

the lungs were the seat of an intense chronic purulent bronchiolitis with tubular bronchiectasis.

Two cases of coronary insufficiency with grossly normal vessels had acute medial necrosis of the superficial coronary arteries. The lesion resembled that described in the aorta which leads to spontaneous rupture.

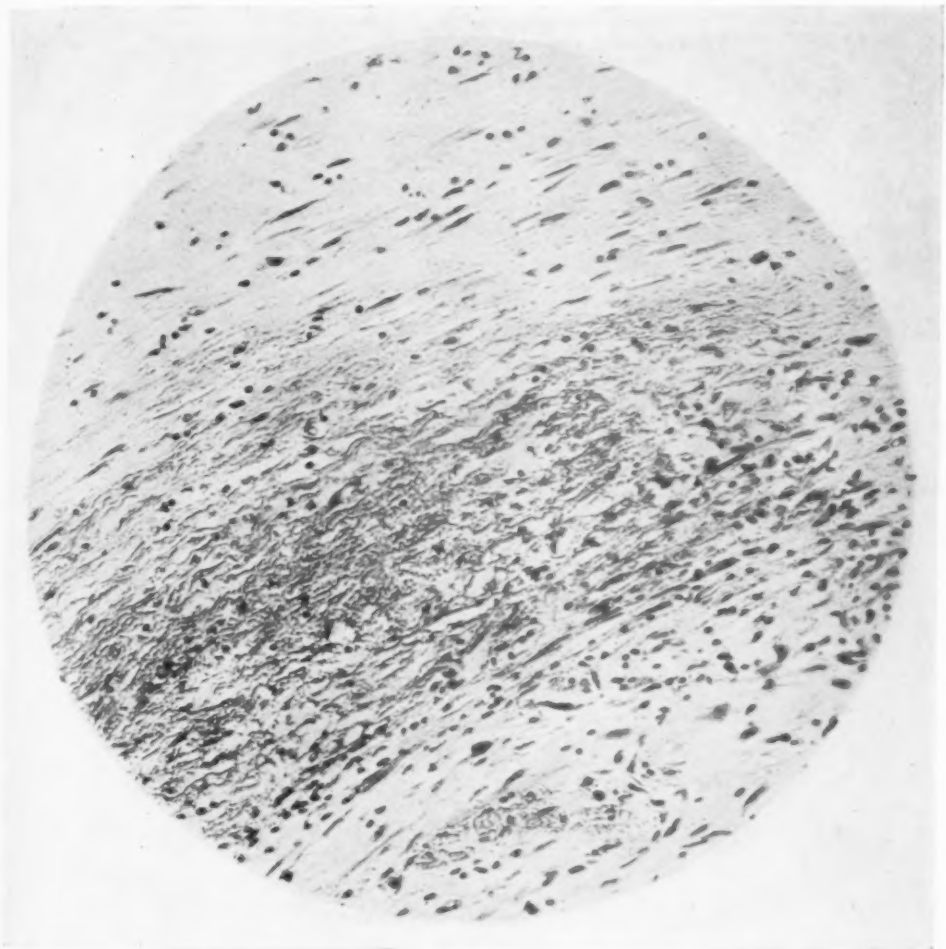

FIG. 3. (Case 31). Acute medial necrosis of the proximal portion of the right coronary artery in a case of acute coronary insufficiency in which the coronary arteries were normal to naked eye inspection.

This type of lesion is generally considered to be toxic and not infectious in nature. In both these cases there was an intense chronic purulent bronchiolitis with tubular bronchiectasis. The myocardial lesion was similar to the changes seen at the periphery of an acute infarction due to coronary thrombosis. Table 3 summarizes the cases of toxic myocarditis.

There was presumptive evidence of a toxic factor producing myocardial damage in six other cases. In two the lesion was similar to that observed in the case of acute pneumonia. One case was an instance of combined syphilis and hypertension. There were two foci of chronic active infection which may have been the source of toxic products, chronic purulent bronchiolitis with bronchiectasis and chronic pyelonephritis. The other case, a child,

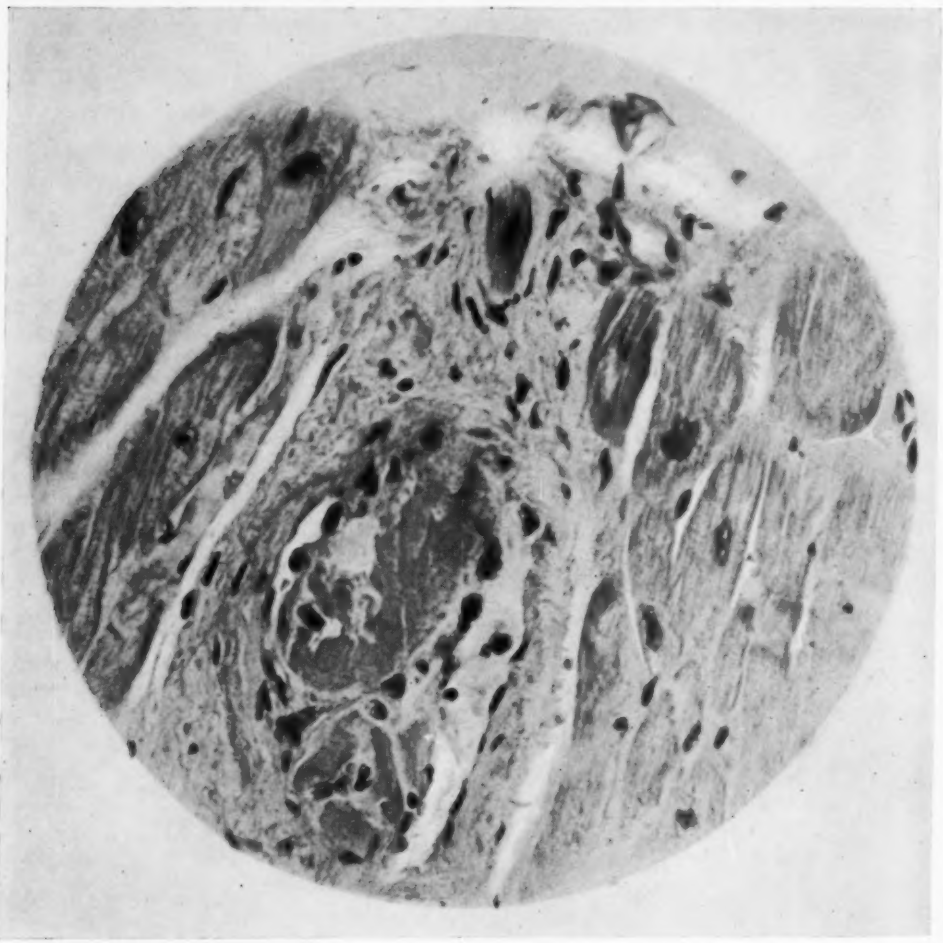

FIG. 4. (Case 6.) Arteriolar thrombi found with acute endocarditis and acute miliary infarctions.

had had a previous infection although none was demonstrable at autopsy. He had entered the hospital with an acute pharyngitis and cervical adenitis and was running a slight fever of 99.6 to 100 degrees. The infection was subsiding and the child gaining weight when a sudden attack of cyanosis and dyspnea occurred with death in a few minutes. The lungs showed no changes. The neck organs were not examined.

TABLE IV

Myocarditides of Presumptive Toxic Nature

Serial No.	Race	Sex	Age	Group	Under Observation	Anatomical Diagnoses	Remarks
14	W.	M.	58	Combined syphilis and hypertension	1 m	Acute miliary infarctions of heart. Acute infarctions of kidneys. Chronic purulent bronchiectasis. Syphilis of aortic arch.	Death in anginal attack.
16	B.	M.	68	Combined syphilis and hypertension	10 m	Acute interstitial myocarditis. Chronic purulent bronchiectasis. Chronic pyelonephritis. Commissural syphilis of aorta.	Congestive failure.
22	B.	F.	75	Acute coronary thrombosis	2 w	Recent coronary thrombosis. Chronic purulent bronchiectasis.	Slight dyspnea for 4 yrs.
25	W.	M.	59	Acute coronary thrombosis	5 m	Recent coronary thrombosis. Chronic purulent bronchiectasis.	Clinically improving.
29	W.	M.	70	Acute coronary insufficiency	13 m	Acute miliary infarctions of heart. Chronic purulent bronchiectasis. Chronic prostatitis.	Compensated for 3 mos.
37	W.	M.	8	Infancy and childhood	2 d	Acute and subacute myocarditis.	Preceding acute pharyngitis, cervical adenitis, cough and low temperature. Clinically recovering.

In two cases the myocardial lesions were of the miliary infarction type. One was a case of combined syphilis and hypertension and one an example of acute coronary insufficiency. Both had the same marked chronic bronchiolitis and bronchiectasis as found in the two previous cases. Multiple kidney infarctions were found in the syphilitic patient. The case of

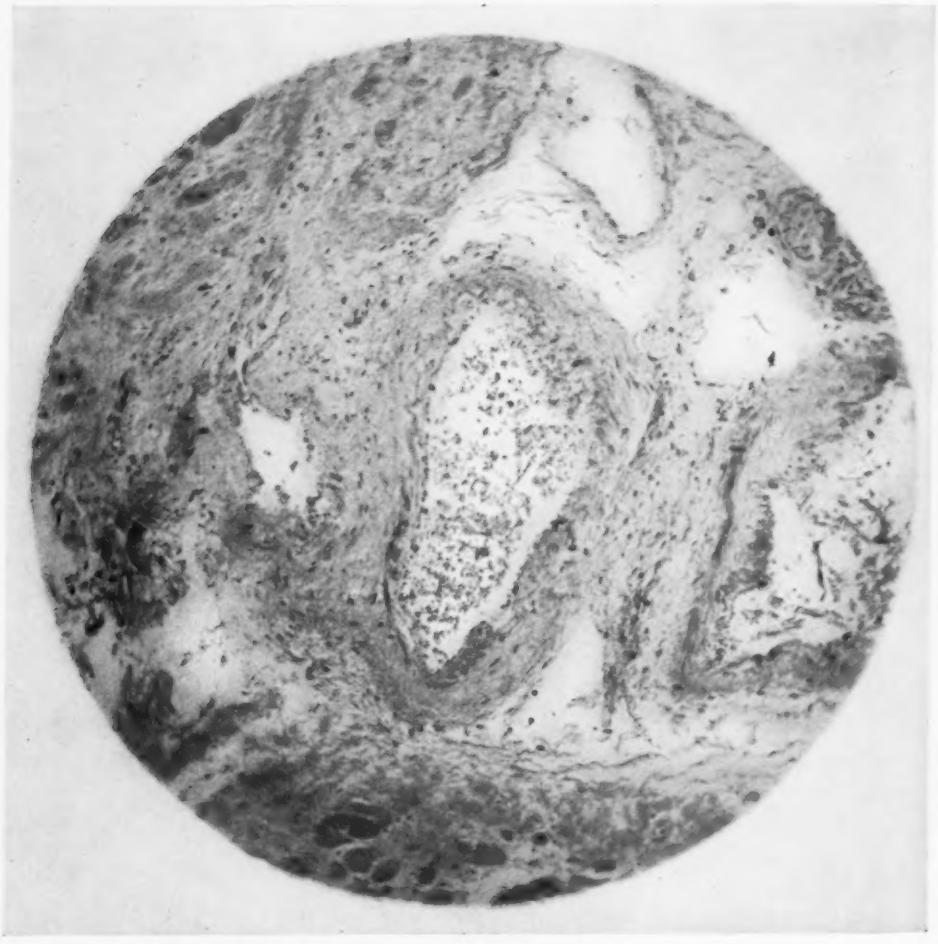

FIG. 5. (Case 30.) Bacterial masses found in the intrinsic arteries of the left ventricle and interventricular wall in a case of acute coronary insufficiency.

acute coronary insufficiency had been compensated for three months. In addition to the chronic pulmonary infection there was a chronic prostatitis.

Two of the cases of acute coronary thrombosis were likewise similar. They also presented the same marked purulent bronchiectasis found in the other cases but again no acute pneumonia was demonstrated. In neither one was there any marked cardiac symptomatology. The first case was a

negro of 75 who had been slightly dyspneic for four years. The second one was a white man who was clinically improving from an anginal attack which had occurred a few days previously. This group of cases of myocarditis of presumptive toxic nature is summarized in table 4.

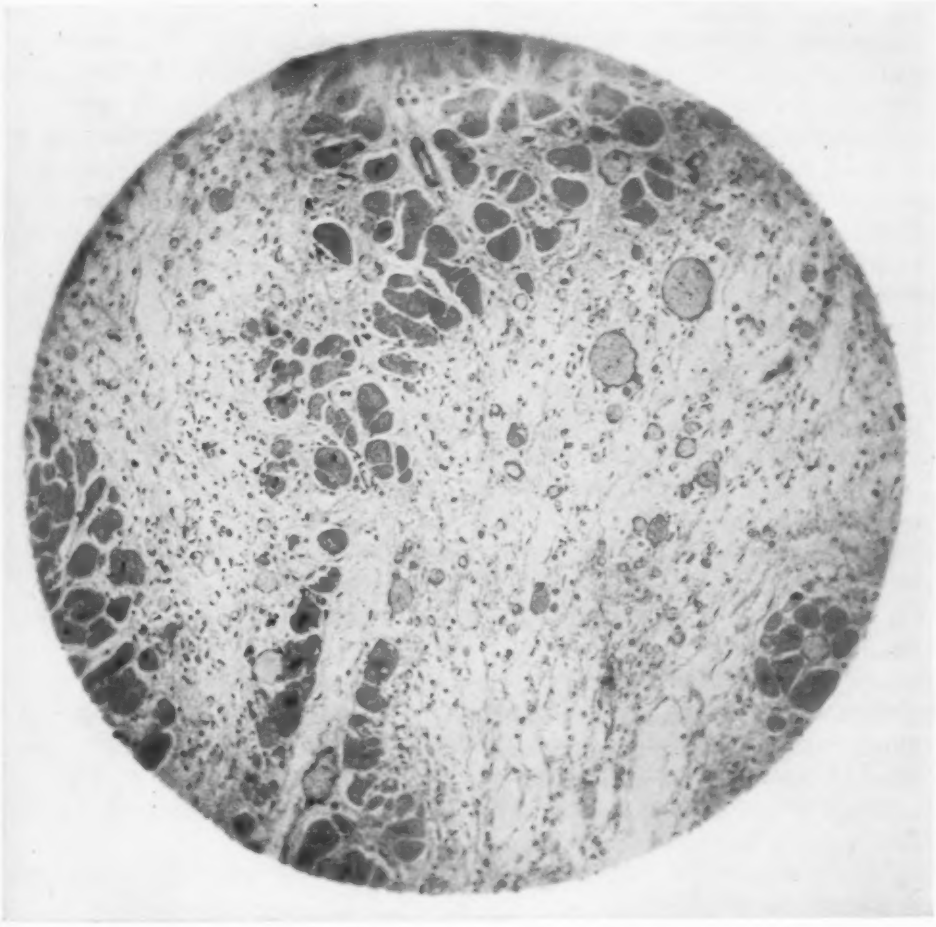

FIG. 6. (Case 6.) Acute miliary infarction.

In the seven remaining cases no factor of infection could be demonstrated. Six were cases of acute coronary thrombosis and one was a child with rickets.

DISCUSSION

The important rôle that infection played in this series of cases was unexpected. There were 14 cases that showed an infection in the myocardium, 12 who exhibited toxic changes in the muscle and there was presumptive evidence of a toxic factor producing myocardial damage in six other cases.

It is generally believed that the most frequent basis of acute cardiac death is arteriosclerosis of the coronary arteries. In this series arteriosclerosis was a minor factor.

The distribution of the acute myocardial lesions offers an anatomical basis for the physiologic mechanism of sudden death. The explanations usually advanced are heart block, and ventricular fibrillation. In the cases of Neisserian infection the lesions were concentrated largely in the interauricular wall affecting the region of the auriculo-ventricular node. Its destruction could well be the basis of a sudden heart block. In the other cases the lesions were largely concentrated in the ventricles, sometimes more on the left than on the right side and occasionally affecting the deep layer of muscle more than the others. Since acutely damaged muscle is hyperirritable, it is possible that the widely distributed lesions may have been foci of ectopic beats and by their summation led to the occurrence of ventricular fibrillation.

Conclusions

1. The pathologic changes in the heart in 41 cases of sudden cardiac death are reviewed.
2. Acute myocardial changes were demonstrated in 39 hearts.
3. Arterial changes of sclerotic nature played the major rôle in six cases only.
4. An infectious process directly affecting the myocardium was present in 14.
5. A toxic process causing myocardial damage, secondary to acute pneumonia was present in 12.
6. Myocardial damage, possibly toxic, was present in six. In five the source was probably a chronic pyogenic pulmonary infection; in the sixth, an acute upper respiratory infection.
7. Myocardial damage of undetermined etiology was present once.
8. Two cases presented no demonstrable changes sufficient to explain the death.
9. An anatomical basis for sudden heart block and ventricular fibrillation is suggested.

PNEUMONIA ASSOCIATED WITH PREGNANCY *

By THEODORE W. OPPEL, M.D., *New York, N. Y.*

PNEUMONIA is one of the rare complications of pregnancy. Among about 15,000 obstetrical patients in the Lying-In Hospital during the past five and one-half years pneumonia has been seen only 15 times during the period of gestation. The marked seasonal and other variations in the natural course of this infection make it extremely difficult to compare the disease occurring in pregnant and non-pregnant women. Most of our knowledge is therefore based on what we know about pneumonia as an infectious disease and on the effect of infectious diseases on pregnancy.

For the present report the larger series of cases of pneumonia during pregnancy will be reviewed and the cases seen in the clinic will be analyzed.

In 1905 Ransdell [1] saw two cases and carefully reviewed the literature on the subject for the previous 200 years. From the German, French, Italian, and English he was able to collect 350 cases. No distinction was made between broncho- and lobar varieties. During the first six calendar months of gestation 144 cases were reported of which 22 per cent died and 52 per cent aborted. During the last three months of pregnancy there were 164 cases of which 30 per cent died and 70 per cent delivered. Forty per cent of infants born at a viable age died. Labor seemed to have an unfavorable effect on the maternal mortality; only 10 per cent of patients who did not go into labor died while 36 per cent of those who delivered did not recover.

A large number of cases of pneumonia associated with pregnancy were seen during the influenza year 1918. These were not the ordinary endemic type of pulmonary disease. The pathological studies of Opie, Blake, Small, and Rivers [2] showed that in addition to a large number of pneumococcal lobar pneumonia cases in 1918 there were more than the usual number of hemolytic streptococcus pneumonias, bronchopneumonias and other forms. Pneumonia was present in all fatal cases of influenza.

From questionnaires Harris [3] collected data on 1,350 cases of influenza associated with pregnancy and found that 50 per cent of them developed pneumonia, half of whom died. The mortality was about 60 per cent during the last trimester of pregnancy and about 40 per cent during the first two. Pregnancy was interrupted in 50 per cent of the pneumonias and the mortality was higher (63 per cent) in those who went into labor than in those who did not (41 per cent). However, not all of the most ill patients aborted, for 38 per cent of the patients died undelivered.

The figures reported by Harris show a generally higher mortality than

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those of Ransdell, a result to be expected since it is usually agreed that influenza increases the seriousness of pneumonia. However, the two series give generally similar results. The mortality was highest late in pregnancy and seemed to be increased by delivery. In both reports there was a higher incidence of pneumonia during the last trimester of pregnancy than during the first two, and the apparent difference is exaggerated by making allowance for the six months in the first two trimesters compared with the three months of the last trimester. This greater incidence of pneumonia toward the end of pregnancy is probably more apparent than real, for as Harris [3] has pointed out, many of the pneumonias in early pregnancy are not seen by obstetricians.

In his recent book, "The Management of the Pneumonias," Bullowa [4] reports 71 cases of pneumonia during pregnancy, and they are divided into those occurring before the seventh month and those after that date. In 31 occurring in the last two months of pregnancy the maternal mortality of 23 per cent and fetal mortality of 28 per cent are lower than during the first seven months of gestation where the maternal mortality was 30 per cent and the fetal mortality was 43 per cent. These results are quite contrary to those of Ransdell [1] and Harris,[3] and the reason for the discrepancy is not clear. Bullowa's series may represent a more complete picture of pneumonia in pregnancy than the others; at least he has a larger proportion of cases occurring early in pregnancy, and it is only reasonable to expect the highest fetal mortality at this time. The differences in maternal mortality could be explained by the natural variation in the severity of the disease.

Bullowa's cases are classified according to the type of organism etiological for the disease and his findings are shown in table 1. They follow the usual distribution seen for pneumococcus pneumonias with the possible exception that there are fewer Type II cases than are usually seen in otherwise healthy women under 50. It is interesting and possibly significant that 22 of Bullowa's 71 cases were not pneumococcal pneumonias. Pneumonia occurring at this age is fundamentally lobar in type, and Cecil [5] found pneumococci responsible for 95 per cent of lobar pneumonia cases. Bronchopneumonia is most often a disease of the debilitated, and it may be that in certain women pregnancy acts as such a condition.

The 15 cases of pneumonia during pregnancy seen in the New York Hospital are summarized in table 2. They occurred from the twenty-fourth to the fortieth week of gestation and all but one of them were lobar in type. Pneumococci were isolated from the sputum of all but one. In this case, although the clinical findings were those of lobar pneumonia *Staphylococcus albus* was the only organism consistently recovered. Type XVIII pneumococcus and a Friedländer bacillus were found in the sputum of the patient with signs and roentgen-ray evidence of bronchopneumonia. There were four Type I cases, one Type II, and one Type III, and one organism was Type VIII or an atypical III. Seven had Group IV pneumococcus, and in the more recent of these where this group was further classified, a Type XVIII was identified. Six patients had positive blood cultures, but in only

TABLE I

Pneumonia Cases Reported by Bullowa

Pregnancy More Than 7 Months			Type	Pregnancy Less Than 7 Months		
Number	Maternal Mortality	Fetal Mortality		Number	Maternal Mortality	Fetal Mortality
7	1	1	I	12	4	5
2	1	1	II	2	1	2
			III	5	3	3
1	0	0	IV			
1	1	1	V			
			VI	1	0	0
2	1	1	VII	1	1	1
1	0	0	VIII	2	0	1
1	0	0	IX	2	1	1
			XII	1	0	0
2	0	0	XIV	1	1	1
			XV	1	0	0
1	0	0	XVII			
1	0	0	XX	1	0	0
1	0	1	XXIII			
11	3	3	Non-pneumococcus	11	1	3
31	7 23%	8 28%		40	12 30%	17 43%

two of these was the culture strongly positive and both of these patients died. The outcome in the others did not seem related to the blood culture findings. Of the five cases for which therapeutic serum was available three were treated. Two had allergic histories, one of whom was found to be sensitive to horse serum.

The most interesting finding on this chart is related to the history of preceding common colds. Ten of the 15 patients had common colds before the onset of their pneumonias, and in two others the data are incomplete, so that there were only three patients with no definite evidence of a preceding respiratory tract infection. Several had colds for two to four weeks before they developed pneumonia. One patient assisted in the care of her husband who had Type I pneumonia 12 days before she developed a fatal case of the same disease.

Four of the 15 patients recovered from pneumonia without going into labor and two others died undelivered. The remaining nine patients delivered during the course of their disease. The day of delivery after the onset of pneumonia is shown in table 3. The much larger series of Ransdell [1] gives a more complete picture than our few cases of the day of disease on which delivery occurs. His results are shown in the same table. Most of his cases delivered within the first six days but delivery apparently can occur at any time. Some allowance should be made for the fact that many cases have recovered by the seventh day of the disease.

TABLE II

Pneumonia Cases Observed at New York Hospital

History Number	Week of Gestation	Type of Involvement	Type of Pneumococcus	Preceding Common Cold	Blood Cultures	Maternal Result	Remarks
44094	24	Lobar	I	Yes	1 col. per c.c.	Recovery	Asthmatic.
143468	28	Lobar	XVIII	Yes	Negative	Recovery	Died 1 mo. later. 4 hrs. P.P. of cryptogenic, erythroblastic splenomegaly.
86086	29	Lobar	I	Yes	385 col. per c.c.	Death	Hay fever and positive skin test. Husband had Type I pneumonia 12 days before patient.
16899	30	Lobar	Group IV	Not known	800 col. per c.c.	Death	
154234	30	Lobar	III	Yes	Negative	Death	
182430	31	Lobar	Group IV	No	Negative	Recovery	Pneumonia during course of severe pyelitis.
42750	34	Lobar	Group IV	Yes	Positive in broth only	Recovery	
58422	36	Broncho	XVIII and Friedländer	Probably	None	Recovery	
56489	36	Lobar	I	No	5 col. per c.c.	Death	85,000 units serum.
117496	36	Lobar	VIII or Atypical III	No	5 col. per c.c.	Recovery	Delayed resolution.
155432	37	Lobar	*Staphylococcus albus*	Yes	Negative	Recovery	
107191	38	Lobar	Group IV	Yes	Negative	Recovery	
13143	39	Lobar	Group IV	Yes	Negative	Death	
97580	40	Lobar	I	Yes	Negative	Recovery	Complicated by otitis media; 82,500 units serum A.P., 57,000 units serum P.P.
28894	40	Lobar	II	Yes	Negative	Recovery	Serum on 2 occasions.
		14 Lobar 1 Broncho	I—4; II—1; III—1; III or VIII—1; Group IV—7	10 Yes		10 Recovery 5 Death	

TABLE III

Day of Pneumonia on Which Delivery Occurred

Day of Pneumonia	1	2	3	4	5	6	7	8	9	10	11+
Number of Deliveries N. Y. H. Series	2	3	1	2	1						
Ransdell's Series	7	18	27	12	16	10	8	3	5	2	13

The effect of pneumonia on the labor and on the fetus can be analyzed from the data in table 4. The estimated week of gestation is listed in column two and the birth weight of the fetus in column three. There is good agreement between the data in these two columns. The duration of the present and of previous labors is recorded in columns four and five. Labor was short when premature infants were born and in most instances was shorter than with the previous pregnancies. In several instances full-term infants were delivered in a surprisingly short time. In others labor seemed to be quite normal, lasting 21 hours in one case. Another patient had mild pains for 82 hours and made no progress. When her pneumonia became severe, labor became very active and she delivered in an hour.

Fetal mortality is generally considered to be high when pneumonia complicates pregnancy. Ransdell [1] states that 41 per cent of infants of viable age die although he does not specify in detail the age and size of the infants. Bullowa [4] had seven deaths among 25 infants born after the seventh month of gestation, a mortality of 28 per cent. Five of these 25 infants had positive blood cultures but three of the infants with positive blood cultures lived. This seems rather surprising as intrauterine infection has been considered one of the major causes of fetal mortality. Toxemia and anoxemia have also been considered harmful to the fetus.

In contrast to the above results the pneumonia seemed to be a relatively unimportant cause of fetal death in our series. Three infants, all of whom weighed less than 1,660 gm., died or were still-born. One of them had a negative blood culture although his mother's blood culture was strongly positive. All of the infants sufficiently large to have a reasonable chance to survive, recovered. There were six of these infants, all of whom weighed more than 2,300 gm. and who were estimated to have had 36 or more weeks of uterine existence. These findings suggest that prematurity is the major cause of fetal mortality in the pneumonia of pregnancy. A larger series of cases will be necessary to verify this finding.

The management of our cases differed little from that given to other pneumonias. Cyanosis was decreased by oxygen administration and most patients delivered in an oxygen tent. There were others, however, in whom cyanosis was too slight to need treatment even during labor. In many writings on the subject emphasis is placed on the avoidance of pituitrin and other drugs which stimulate uterine contractions in the treatment of the distention of the pneumonia of pregnancy. In only one of our cases was dis-

TABLE IV

Duration of Labor and Fetal Mortality at New York Hospital

History Number	Week of Gestation	Birth Weight of Fetus	Duration of Labor	Duration of Preceding Labors	Fetal Result	Maternal Result	Remarks
44094	24	760	$2^{46}/_{60}$	1—24 hours 2— 3—10 hours 4—12 hours	Stillborn	Recovery	
143468	28		Did not deliver during pneumonia recovery			Recovery	
86086	29	1650	$^{45}/_{60}$	1—Version 2—Abortion 2 months 3—Abortion 2½ months 4—Forceps	Died 1 day old	Death	Maternal blood culture 385 col. per c.c. Fetal blood culture negative.
16899	30		Died undelivered			Death	
154234	30	1660	$3^{7}/_{60}$	None	Died 1 day old	Death	Maternal blood culture negative.
182430	31		Did not deliver during pneumonia			Recovery	
42750	34		Did not deliver during pneumonia			Recovery	
58422	36		Did not deliver during pneumonia			Recovery	
56489	36		Died undelivered			Death	
117496	36	2320	$1^{49}/_{60}$	1—6 hours 2—6 hours 3—6 hours	Lived	Recovery	
155432	37	2430	$1^{19}/_{60}$	None	Lived	Recovery	
107191	38	3240	$21^{42}/_{60}$	1—24 hours 2—24 hours 3—Abortion 3 weeks	Lived	Recovery	
13143	39	3145	1	1—9 hours	Lived	Death	Mild labor without progress 82 hours before onset of real pains.
97580	40	3440	$7^{19}/_{60}$	1—22 hours 2—12 hours	Lived	Recovery	
28894	40	2930	$5^{32}/_{60}$	1—7 hours 2—3–4 hours 3—3–4 hours 4—3–4 hours 5—3–4 hours 6—3–4 hours 7—3–4 hours	Lived	Recovery	

tention marked before delivery and it was readily relieved by enemas and turpentine stupes. It is also considered advisable to delay labor since the mortality seems to be highest in patients who deliver. It is reasonable to expect that the work required for delivery would lessen the chances of recovery of any pneumonia patient. It seems evident from reviewing these cases, however, that the obstetricians have little control over the onset of uterine contraction and that most patients go into labor in spite of precautions to prevent it.

There are scant data from which to evaluate the use of serum in the pneumonia of pregnancy. Bullowa [4] believed that some mothers and infants survived as a result of serum treatment, and recommends its use as early as possible in the disease. In 27 cases in which serum was given the maternal mortality in his series was 37 per cent. Doubtless many of these were very ill patients for in the cases not given specific serum the mortality was 20 per cent, and only 30 per cent of the pneumococcal pneumonias who did not get serum died. These results are rather disappointing but the series is much too small to give a real picture of the value of therapeutic serum. Bullowa observed no harmful effects from serum and its administration did not induce labor in any case.

In addition to the cases just discussed, five of our patients developed pneumonia early in the puerperium. Four of these had common colds at the time of delivery and several of them may have had early pneumonia. All had non-operative deliveries without anesthesia. One was found to be febrile immediately post-partum; one had a chill 12 hours after delivery; another had a chill and bloody sputum on the first post-partum day; a fourth patient had signs of consolidation 17 hours after delivery; and a fifth had similar signs on the fourth post-partum day. All patients recovered except one who died of Type II pneumococcus bacteremia on the fifth post-partum day.

These patients were separated from the previously described group because the presence of pneumonia was not established before delivery. Possibly some of these should have been considered pneumonia during pregnancy in which the patients went into labor early in the disease. It is interesting to note that pneumonia was diagnosed in the first five days of the puerperium in one-third as many instances as it was seen during the entire 40 weeks of pregnancy and that it was preceded by a common cold in almost every instance.

Summary and Conclusions

In summarizing this study we find that pneumonia is an infrequent but serious complication of pregnancy. Once it has developed it is very similar to pneumonia in non-pregnant women. It is difficult to establish that the mortality is appreciably altered by the presence of pregnancy. Patients may die or recover undelivered, but in the majority of instances they go into

labor. Labor is apt to develop early in the disease but may begin late. It is frequently of short duration but may run the usual course. If the infant is of sufficient size and age, it will probably live.

Common colds usually precede the development of pneumonia during pregnancy and pneumonia is apt to develop during the puerperium in patients who have common colds at the time of labor. The adequate treatment of a common cold during pregnancy is an important way of preventing pneumonia during pregnancy and the puerperium.

The management of the pregnant patient with pneumonia is essentially the same as the management of any pneumonia patient. There are insufficient data for determining the value of specific treatment in the therapy of the pneumonia of pregnancy.

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UNSUSPECTED CORONARY THROMBOSIS IN PATIENTS WITH HEMIPLEGIA—A CLINICAL STUDY *

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In a recent report [1] reviewing 1000 consecutive, unselected autopsies for the incidence of coronary thrombosis in patients dying with a diagnosis of a cerebrovascular accident, it was found that of the 1000 cases, there were 107 with either cerebral hemorrhage, cerebral thrombosis or cerebral embolism. Of these 107, there were 12 that had a coronary thrombosis in addition to the cerebral lesion; but the cardiac condition had not been diagnosed antemortem in a single case.

During the study of the 1000 autopsies, there were found 41 cases of established coronary thrombosis. Since 12 of these were undiagnosed and were complicated by a cerebral lesion, it would appear that 29 per cent of the cases with coronary thrombosis were masked by the predominating symptoms of an acute cerebral catastrophe. In the previous report it was pointed out that these figures vary considerably from those in the literature. Mention was also made that the usual reports deal with the incidence of cerebral embolism as a complication in patients known to have coronary thrombosis, whereas the report under discussion was concerned with the frequency of unsuspected, undiagnosed coronary thrombosis in patients with an antemortem diagnosis of cerebral thrombosis, cerebral hemorrhage or cerebral embolism.

In view of the autopsy findings in the previous report and because the method of study yielded different figures from those usually encountered in the literature, it was decided to study a group of clinical cases in an attempt to establish the true relationship between coronary thrombosis and cerebral embolism.

Method of Study

All patients presenting themselves with evidence of a cerebrovascular accident, chiefly hemiplegia, were studied in the usual manner, and in addition routine electrocardiographic tracings with four leads, teleoroentgenograms of the heart when possible and occasionally the venous pressure were recorded. Patients that succumbed to their illness were submitted to postmortem examination when feasible. The material to be presented was obtained from three different sources:

† I. From the neurological service of the late Dr. Clarence A. Patten at the Philadelphia General Hospital.

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† Through the courtesy of the late Dr. Clarence A. Patten.

† II. From the neurological service of the late Dr. Clarence A. Patten at the Lankenau Hospital.

‡ III. From the medical service of Dr. George M. Piersol at the Graduate Hospital, University of Pennsylvania.

Coronary Thrombosis Unsuspected in Patients with Hemiplegia

There were 66 patients studied; 25 did not recover from their illness and 15 of these had a postmortem examination.

Material obtained from	No. of cases with a cerebrovascular accident	No. of foregoing cases with coronary thrombosis	Percentage with cerebral and cardiac lesion
Lankenau Hospital	11	1	9%
Philadelphia General Hospital	40	5	12%
Graduate Hospital	15	2	13%
Above combined (total)	66	8	12.1%

It will be noted from the above table that 12.1 per cent or 8 of the 66 cases studied, had coronary thrombosis in addition to the cerebral lesion.

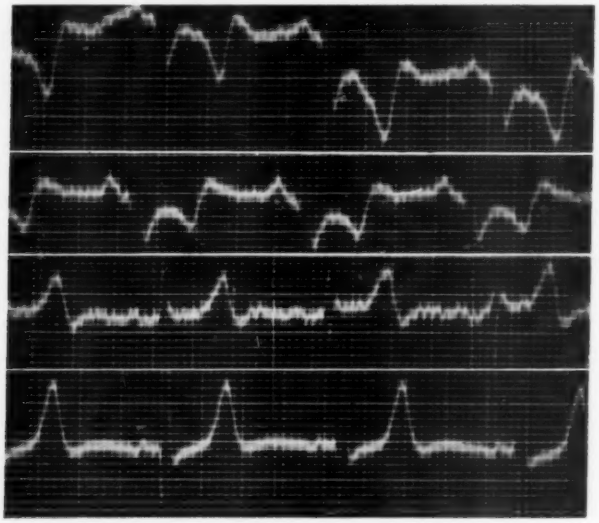

Fig. 1. Electrocardiograph tracing in Case 1.

Rate 70.
P–R 0.16 second.
QRS 0.08 second.
T_1, T_2 exaggerated in size and deeply inverted.

† Through the courtesy of the late Dr. Clarence A. Patten.
‡ Through the courtesy of Dr. George M. Piersol.

The incidence of the association of the two lesions varied slightly at each hospital. The diagnosis of coronary thrombosis was verified by autopsy in four instances. Two of the cases of coronary thrombosis were of recent origin with some myomalacia. The other two cases were of long standing as evidenced by healing and the presence of mural thrombi. In all four cases it was difficult to state whether the cerebral lesion was a thrombosis or embolism. One of the cases wherein the cardiac lesion was of long standing was difficult to classify antemortem, in that there was some uncertainty as to whether the changes in the electrocardiographic tracings were due to an old, healed coronary thrombosis, or due to a marked coronary sclerosis.

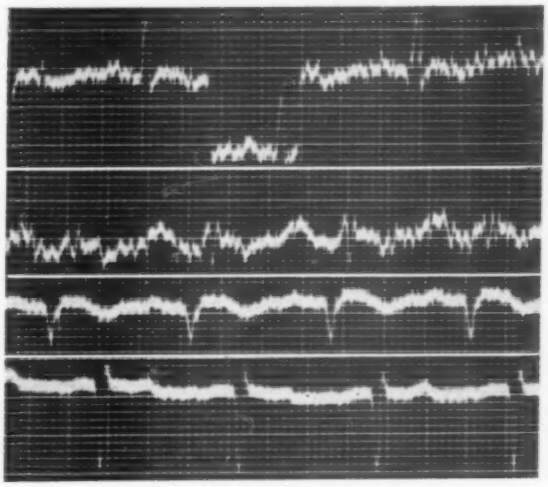

FIG. 2. Electrocardiographic tracing in Case 2.

Rate 90.
N. S. R.
P–R—prolonged.
QRS 0.08.
T_1, T_2, T_3 inverted.

There was nothing characteristic about the history or any of the clinical findings which would lead one to suspect the presence of coronary thrombosis. Six of the patients were males and they were from 50 to 60 years of age. Some of the patients were aphasic when admitted to the hospital, thereby making it necessary to rely upon information obtained from other sources. Occasionally, a history was obtained of previous acute precordial or substernal pain, which the patient had failed to mention during the first interrogation. One of the eight patients with both coronary thrombosis and cerebral thrombosis gave a definite history of having had coronary thrombosis one year previous. None of the eight cases was diagnosed as having coronary thrombosis until the routine studies were completed. One

of the other patients in the group of 66 gave a history of an antecedent coronary thrombosis without demonstrable evidence at the time of the study.

It was pointed out in the previous report [1] that perhaps the cerebral lesion is induced by the fall in blood pressure subsequent to the coronary thrombosis, or that both the cerebral and cardiac lesions are merely coincidental to the same pathological process in the respective arteries. Attention has been called to painless coronary thrombosis by East et al.,[2] and recently by Boyd and Werblow.[3] Parkinson [4] states that dyspnea may take the place of pain when coronary thrombosis develops in a patient with cardiac decompensation.

Case Reports

While it was previously stated that there is nothing characteristic in the history or clinical findings to make one suspect coronary thrombosis in patients with hemiplegia, it would seem fitting to present a typical example of a patient with both a cerebral and a cardiac lesion, and of another with a cerebral lesion without evidence of coronary thrombosis.

Case 1. H. M., a white male, aged 61 years, was admitted to the service of Dr. Piersol at the Graduate Hospital, December 28, 1934. Physical examination revealed a right-sided hemiplegia, and the patient manifested difficulty in swallowing. Examination of the heart was essentially negative except for some enlargement of the area of precordial dullness to the left. The blood pressure 230 systolic and 140 diastolic. The past history was inconsequential other than the occurrence of a mild left-sided hemiparesis in June 1934, with complete recovery. Routine electrocardiographic tracing revealed evidence of unsuspected coronary thrombosis. The patient was very ill, but recovered and was discharged February 3, 1935.

Case 2. J. D., a white male, 53 years of age, was admitted to the service of Dr. Piersol at the Graduate Hospital, February 7, 1935. Physical examination revealed a left-sided hemiplegia. Examination of the heart was essentially negative. The blood pressure was 170 systolic and 90 diastolic. Past history—"Stroke in October 1934." Frequent attacks of "pain in chest." Routine electrocardiographic studies revealed strain on the left ventricle and coronary disease. Uneventful recovery. Discharged February 20, 1935.

It is seen from the likeness of the two cases presented that without detailed, routine studies of the heart, it is most difficult to ascertain which case of hemiplegia is likely to be complicated by an unindicated coronary thrombosis. In view of these findings and those previously reported, it appears that we have not been aware of the frequency of coronary thrombosis in patients with hemiplegia. This seems to be particularly true in the white male 40 or more years of age.

In the autopsy material the incidence was 12 cases out of 107, or 11.2 per cent. The studies on the clinical material reveal an incidence of 12.1 per cent. While these two studies tend to substantiate one another, the results differ from those of other writers. Parkinson et al.[4] refer to embolism as a complication of coronary thrombosis and out of 83 cases autopsied,

found cerebral embolism in one case, an incidence of 1.2 per cent. Meakins and Eakin [5] report the autopsy findings of 62 cases with coronary occlusion and state that 6.4 per cent had a cerebral thrombosis. Conner and Holt,[6] in reviewing 287 cases with coronary thrombosis, state that 14 had developed cerebral embolism and two developed signs of cerebral thrombosis many months after the attack of coronary thrombosis. In their series the incidence was approximately 5 per cent.

Summary

Sixty-six patients with hemiplegia were studied for the incidence of coronary thrombosis. It was found that 8 or 12.1 per cent of these patients with hemiplegia also had coronary thrombosis and that the latter lesion would not have been diagnosed were it not for the routine inclusion of detailed heart studies in the examination of all patients with hemiplegia, irrespective of history or clinical findings. While these figures compare favorably with the previously reported incidence of 11.2 per cent based on autopsy material, these results vary considerably from those of other workers.

Although there is nothing characteristic about the history or clinical findings of the hemiplegic who is prone to have an unindicated or latent coronary thrombosis, the incidence is definitely greater in the white male beyond 40 years of age. The majority are between 50 and 60 years. It was pointed out that the cerebral lesion may be induced by the drop in blood pressure secondary to the coronary thrombosis, or that both lesions may be due to the same pathological process in the respective arteries. Mention was also made of the atypical forms of coronary thrombosis. There may be practical value in recognizing the association between coronary thrombosis and cerebral embolism from a therapeutic and prognostic point of view.

The author acknowledges indebtedness to the late Dr. Clarence A. Patten for his cooperation in obtaining the material used for this study.

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THE DEVELOPMENT OF ARTERIOSCLEROSIS IN THE DIABETIC, BASED ON THE STUDY OF A GROUP OF PATIENTS DURING TEN TO THIRTEEN YEARS *

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Both clinical and pathologic data support the view that vascular disease of the atherosclerotic type occurs earlier and is more extensive in the diabetic patient. Now that the proper use of insulin can almost eliminate uncomplicated acidosis as a cause of death and has greatly improved the status of the diabetic patient with an infection, attention, at the present time, is being directed toward the reduction of the intensity of atherosclerosis. The involvement of the muscular arteries, particularly the coronaries and those of the extremities, is responsible for the majority of deaths in older diabetics. Whatever the pathogenesis of this process may be, the majority opinion agrees that it is caused by the diabetes. The Virchow-Aschoff cholesterol imbibition theory of arteriosclerosis, the production of experimental atherosclerosis and the disturbed cholesterol and fat metabolism in diabetes, together form the background for the conception that atherosclerosis in the diabetic is caused by altered fat and cholesterol metabolism. For this reason the use of large amounts of fat in the diabetic diet has been considered by some physicians to be a possible etiologic factor in the production of premature atherosclerosis.

The observations which form the basis of this article are a continuation of similar studies made in 1924 [1] and in 1927.[2] In 1924 the lower extremities of a group of diabetic patients were examined for calcification of the arteries by means of roentgenograms; in 1927 the same group was restudied by the same method, and additional patients were observed. Sixty-three per cent of 167 patients beyond the age of 40 were found to have a degree of calcification that could be detected roentgenologically. In a group of 121 non-diabetic people of the same age, 28 per cent had such calcification. Further, it was believed that the data showed that incomplete control of the diabetes was the most influential factor in the production of this calcification. It also appeared that uncontrolled diabetes over a period of five years was sufficient to produce calcification even in younger diabetic patients. At that time higher fat diets were being used than at present. However, they were not as excessively high in fat as those advocated by

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From the Out-Patient Department of the Buffalo General Hospital.

others during that period. The carbohydrate content was usually from 50 to 100 grams, protein, one gram per kilo of body weight, and fat, 130 to 170 grams daily. The patients in this study were on this moderately high fat diet until 1933–1935, when the carbohydrate content was increased somewhat and the fat reduced. During 1936–1937, we were able to re-study 52 of the patients in the original groups. In addition the adequacy of the circulation of the lower extremities was determined by clinical methods. Particularly we were interested to determine, if possible, the influence of the diet, and further to get additional information on the effect of the methods by which the diabetes had been controlled. Nearly all of these patients were observed with sufficient regularity so that the examiner gained a good idea as to their reliability and coöperativeness. The ratings as to the control of the diabetes were given rather arbitrary designations such as had been employed in the previous studies. The words *excellent, good, fair,* and *poor* lack the precision which should characterize accurate investigation, but in a long-term observation such as this it is not possible to get more than a general idea with regard to a patient's behavior. It is believed, however, that a physician who personally comes in contact with patients over a long period gets an opinion that is significant. The contributors to this study made their observations independently before the complete data were organized. One of us (B. D. B.) cared for the patients and rated them as to the control of the diabetes. The studies of the circulation of the lower extremities were made in The Peripheral Vascular Clinic by a second observer (J. S. R.) and the roentgenograms were interpreted by a third (E. C. K.). The designations of the degree or extent of visualization of the calcified arteries by roentgenography were the same as was used in previous articles. The patients were divided into three groups and were arranged in chronological order according to the duration of the diabetes.

Group I (table 1) contains 20 patients who were believed to have had their diabetes under *good* or *excellent* control throughout most of their diabetic life. Thirteen were women and seven were men. The average age was 59. Only three of the patients had a stout habitus; the others were either thin or of average body conformation. The average estimated duration of the diabetes was 13.7 years and the average number of years on insulin was 11.7. Three of them did not require insulin and the average daily dose for the others was 32 units. None of the patients had a diastolic blood pressure that exceeded 90 mm. at any time. In 1927 the systolic blood pressure was 150 mm. or over in seven, whereas in 1936–1937 this was the case in nine. Only two of the patients, both women whose ages exceeded 75 years (Cases 12 and 15), showed extensive calcification of the leg arteries; these also showed a marked degree of circulatory deficiency of the lower extremities. Five of the group (Cases 1, 5, 10, 11 and 13) showed questionable deficiency of the circulation of the legs and feet by the method employed, and Cases 6, 9, 19 and 20 had slight but definite objective impairment.

TABLE I (GROUP I)

Control of diabetes estimated as *excellent* or *good* throughout. Averages: Age, 59 years; probable duration diabetes, 13.7 years; years on insulin, 11.7; daily insulin dosage, 32 units. Thirteen women, seven men.

Case No.	Age	Sex	Habitus	Probable Duration Diabetes	Insulin		Blood Pressure (mm.)						Calcification (Roentgen-ray) Feet—Legs			Circulation of Lower Extremities							Clinical Comments
							1924		1927		1936–37												
				Years	Yrs.	Units (24 hrs.)	Sys.	Dias.	Sys.	Dias.	Sys.	Dias.	1924	1927	1936–7	Dorsalis Pedis Pulses	Posterior Tibial Pulses	Claudication	Trophic Changes	Dependent Rubor	Elevation Pallor	Circulation Deficiency	
1	67	F.	Stout	22	13	24	108	80	155	90	130	70	0	0	0	3+	2+	0	0	±	±	±	Cellulitis of foot several times.
2	61	F.	Average	19	14	55			185	50	170	90	0	0	0	−	−					−	Pulmonary and renal tuberculosis.
3	73	F.	Average	15	13	26			130	80	190	90		0	0	2+	2+	0	0	0	±	0	
4	47	F.	Average	15	14	28			125	80	110	75		0	0	3+	3+	0	0	0	±	0	Coma, 1924.
5	47	F.	Average	15	13	16			110	80	120	80		0	0	4+	4+	0	0	±	±	±	Coma, 1924.
6	42	F.	Average	15	13	22			125	85	135	80		0	0	0	4+	+	0	±	+	+	Coma, 1925. Feet very sensitive to cold.
7	62	F.	Thin	15	14	40	145	80			133	70	0	0	±	3+	3+	0	0	0	±	0	Coma, 1925.
8	60	F.	Average	15	−	−	150	70	165	75	180	70	0	0	0	2+	2+	0	0	0	0	0	Hyperthyroidism, 1936.
9	76	F.	Average	14	13	21			150	90	205	80		0	0	+	+	0	0	+	0	+	

TABLE I (GROUP I)—*Continued*

Case No.	Age	Sex	Habitus	Probable Duration Diabetes	Insulin		Blood Pressure (mm.)						Calcification (Roentgen-ray) Feet—Legs			Circulation of Lower Extremities							Clinical Comments
							1924		1927		1936–37												
				Years	Yrs.	Units (24 hrs.)	Sys.	Dias.	Sys.	Dias.	Sys.	Dias.	1924	1927	1936–7	Dorsalis Pedis Pulses	Posterior Tibial Pulses	Claudication	Trophic Changes	Dependent Rubor	Elevation Pallor	Circulation Deficiency	
10	67	M.	Stout	14	12	28			140	85	130	70		0	0	2+	2+	0	0	0	+	±	Coronary occlusion, 1936.
11	40	M.	Thin	14	13	50					120	80		0	0	+	4+	0	0	0	2+	±	
12	78	F.	Thin	12	9	18			170	90	180	90		0	2+	0	+	+	+	+	+	3+	Coronary occlusion, 1928.
13	65	M.	Stout	11	—	—			110	65	135	75		0	+	0	4+	0	0	±	±	±	Very mild diabetes.
14	65	F.	Average	11	9	6	135	80	140	85	150	95	0	0	0	3+	2+	0	0	0	+	0	
15	83	F.	Average	11	10	15			225	90	230	60		3+	3+	0	0	?	0	+	+	2+	Coronary occlusion, 1936. Died, 1937.
16	65	F.	Average	11	—	—			150	85	160	90		0	0	2+	2+	0	0	0	0	0	Unstable blood pressure.
17	62	M.	Average	11	9	23			160	80	190	90		0	0	3+	3+	0	0	0	0	0	
18	50	F.	Average	11	10	65			130	80	115	70		0	0	+	+	0	0	0	±	0	Coronary occlusion, 1936.
19	35	M.	Thin	11	10	60			130	80	105	70		0	0	0	3+	0	0	+	+	+	
20	40	M.	Average	11	10	42			120	80	125	75		0	0	0	4+	0	0	+	+	+	

TABLE II (GROUP II)

Control of diabetes estimated as *fair* or *poor* throughout. Averages: age, 55 years; probable duration diabetes, 14.7 years; years on insulin, 9; daily insulin dosage, 36 units. Fourteen women, nine men.

Case No.	Age	Sex	Habitus	Probable Duration Diabetes	Insulin		Blood Pressure (mm.)						Calcification (Roentgen-ray) Feet—Legs			Circulation of Lower Extremities							Clinical Comments
							1924		1927		1936–37												
				Years	Yrs.	Units (24 hrs.)	Sys.	Dias.	Sys.	Dias.	Sys.	Dias.	1924	1927	1936–7	Dorsalis Pedis Pulses	Posterior Tibial Pulses	Claudication	Trophic Changes	Dependent Rubor	Elevation Pallor	Circulation Deficiency	
1	78	F.	Stout	21	11	18			160	90	170	80		2+	4+	3+	0	0	0	+	+	2+	Retinitis.
2	72	M.	Average	18	13	24			150	100	180	100		3+	4+	±	0	0	0	2+	2+	3+	Died cerebral thrombosis.
3	82	F.	Average	17	10	20	145	80	165	90	180	100		+	3+	+	0	0	0	2+	2+	2+	Congestive heart failure.
4	44	M.	Stout	17	13	70			120	80	130	100		+	2+	2+	2+	0	0	0	±	0	
5	42	F.	Stout	17	13	40	80	54	120	85				0	3+								
6	69	M.	Stout	17	13	36			120	80	150	80		+	3+	0	0	2+	+	2+	2+	3+	Peripheral neuritis.
7	59	M.	Stout	17	12	60			140	80	140	90		3+	3+	+	0	0	+	+	2+	2+	
8	55	M.	Average	16	14	50			130	75	140	80		0	3+	0	0	0	+	3+	3+	3+	Took insulin irregularly.
9	71	M.	Stout	16	—	—	130	70	130	80	170	80	2+	3+	4+	+	0	0	0	+	+	+	Died pulmonary tuberculosis.
10	59	M.	Average	15	13	50	106	58	106	58	120	80	0	0	3+	0	0	±	0	+	+	2+	Developed gangrene; retinitis.
11	68	F.	Stout	15	9	18	185	90	190	85	170	90		±	4+	0	0	+	+	±	+	3+	
12	74	F.	Stout	14	4	16	110	80	170	90	145	85	+	2+	3+	0	0	0	0	+	+	2+	Coronary occlusion, 1935.

TABLE II (GROUP II)—*Continued*

Case No.	Age	Sex	Habitus	Probable Duration Diabetes	Insulin		Blood Pressure (mm.)						Calcification (Roentgen-ray) Feet—Legs			Circulation of Lower Extremities							Clinical Comments
							1924		1927		1936–37												
				Years	Yrs.	Units (24 hrs.)	Sys.	Dias.	Sys.	Dias.	Sys.	Dias.	1924	1927	1936–7	Dorsalis Pedis Pulses	Posterior Tibial Pulses	Claudication	Trophic Changes	Dependent Rubor	Elevation Pallor	Circulation Deficiency	
13	56	M.	Stout	14	13	54			135	90	152	80		0	±	+	4+	0	±	+	2+	+	
14	68	F.	Stout	13	7	30			135	75	210	80		0	3+	±	0	0	+	+	+	2+	Peripheral neuritis.
15	23	F.	Stout	13	12	50					105	90		0	4+	3+	0	0	±	0	0	0	Pulmonary tuberculosis, 1936.
16	59	F.	Average	13	10	20			135	95	160	90		0	0	4+	0	0	0	±	0	0	Took insulin irregularly.
17	66	F.	Stout	13	—	—	135	80			170	105		0	3+	2+	+	0	0	0	0	0	Congestive heart failure.
18	53	F.	Stout	13	12	60			140	90	140	90		0	0	4+	4+	0	0	0	0	0	Syphilis; varicose ulcers.
19	74	F.	Stout	13	—	—	180	90	180	90	160	90	0	0	+	0	0	+	±	+	+	2+	
20	50	F.	Stout	12	—	—			132	88	120	70		0	+	2+	4+	0	0	0	±	0	
21	23	F.	Stout	12	11	42					150	80		0	3+	+	0	+	0	+	0	2+	Peripheral neuritis; died of infection, 1937.
22	60	M.	Average	12	11	22	120	80	125	80	125	80		0	+	2+	4+	0	0	0	0	0	
23	59	F.	Stout	10	8	15			160	80	160	90		0	0	0	2+	0	0	±	±	+	Peripheral neuritis.

Group II (table 2) was comprised of the patients who were regarded as uncoöperative. The average age was 55, inclusive of two patients (Cases 15 and 21) who were 23 years old; if these had been omitted the average age would be about the same as that of the patients in Group I. The ratio of men to women was also about equal in the two groups. A stout body habitus predominated in this uncoöperative group; at the present time, however, a number of these patients are thin because of uncontrolled diabetes. The average patient in this group has had diabetes a year longer and has taken insulin two years less than the average patient in Group I. The dosage of insulin was slightly greater. Insulin was not given to three of the patients because it probably would only have increased their appetites. Nine of the 23 patients in this group had been under observation in 1924; two of them had an increase in the systolic blood pressure at that time without any essential change since. In 1927, seven of the patients had systolic blood pressures that were 150 mm. or more. In 1936–1937, 11 patients had an increase in the systolic blood pressure. During this 10 year period, however, there was no noteworthy change in the diastolic blood pressure. Calcification of the arteries of the legs either appeared or was intensified in 19 of the 23 patients. This is conspicuously shown by an analysis of the findings in the roentgenograms taken in 1927 and in those taken in 1936–1937. Fifteen of the 22 patients upon whom we were able to make clinical observations of the circulation of the lower extremities showed definite evidence of impairment of the peripheral circulation.

Group III (table 3) is made up of the patients whose diabetes was inadequately controlled for a period before insulin treatment. The majority of these patients had undergone serious under-nutrition, either from low caloric diets or as a result of severe diabetes. With one exception, Case 2, the control of the diabetes has been excellent since insulin treatment was begun. The average age of the five women and four men in this group was 65. The average estimated duration of the diabetes was 19 years. The average time of insulin therapy was 13 years and the daily insulin requirement, 49 units. One patient had an elevated diastolic blood pressure in 1927 and two in 1936–1937. The systolic blood pressures exceeded 150 mm. in three instances in 1927; these were found to be still more elevated ten years later. Five of the patients of this group were observed in 1924. At that time three of them had calcification of the arteries of the feet and legs. In 1927 the intensity of this calcification had not changed. In 1936–1937 all but two of the patients in this group had developed evidence of calcification. One, Case 6, a physician, had lived on a high fat diet from 1918 to 1926 when insulin became necessary. At that time he was again placed on a high fat diet on which he remained for eight additional years. We were able to study clinically the peripheral circulation of the lower extremities in eight of the nine patients. Only two of them showed a marked disturbance; in the others the disturbance was only slight. The patient who

TABLE III (GROUP III)

Control of diabetes inadequate before insulin but good since. Averages: age, 65 years; probable duration diabetes, 19 years; years on insulin, 13; daily insulin dose, 49 units. Five women, four men.

Case No.	Age	Sex	Habitus	Probable Duration Diabetes	Insulin		Blood Pressure (mm.)						Calcification (Roentgen-ray) Feet—Legs			Circulation of Lower Extremities							Clinical Comments
							1924		1927		1936–37					Dorsalis Pedis Pulses	Posterior Tibial Pulses	Claudication	Trophic Changes	Dependent Rubor	Elevation Pallor	Circulation Deficiency	
				Years	Yrs.	Units (24 hrs.)	Sys.	Dias.	Sys.	Dias.	Sys.	Dias.	1924	1927	1936–7								
1	68	F.	Stout	23	14	46	130	80	160	85	175	80	2+	2+	3+	±	0	0	0	0	0	+	Retinitis.
2	70	F.	Average	20	14	90	140	90	180	100	210	120	0	0	2+	0	0	+	+	+	+	2+	Poor control of diabetes in recent years.
3	58	F.	Stout	20	14	60	75	60	120	70	150	80	0	0	+	0	0	+	+	2+	2+	3+	Cerebral occlusion, 1935.
4	68	F.	Average	19	14	58	86	72			150	80	0	0	0								Died coronary occlusion, 1937.
5	59	M.	Stout	19	13	44	145	90	160	90	205	105	2+	2+	3+	2+	2+	0	±	+	+	+	Coronary occlusion, 1937.
6	63	M.	Average	20	12	32			120	70	140	70		0	0	3+	3+	0	0	±	±	±	Diabetes well controlled by diet from 1918–1926.
7	62	F.	Stout	19	12	30			120	90	125	80		0	+	2+	0	0	0	0	+	+	
8	64	M.	Stout	17	12	20	110	70	110	80	130	80	+	+	3+	0	4+	0	0	+	+	+	Carcinoma of colon, 1933.
9	69	M.	Stout	14	9	60			120	80	125	80		0	3+	0	2+	0	0	+	2+	+	Coronary occlusion, 1936.

showed the least disturbance, Case 6, had no calcification. Three of the patients, one man and two women, developed cardiac infarction.

Coronary Occlusion

In the three groups of this series, seven of the patients had coronary occlusion; two of these died after these observations were made. Of the patients studied in 1924 and 1927, who could be followed, 10 were believed to have died of cardiac infarction. On reviewing their case histories together with those of the seven instances of infarction in the present series, it was found that seven patients had no calcification of the arteries of the lower extremities and six had hypertension. The outstanding characteristic of this group was stoutness which was present in 15 of the 17 patients. In this small number of patients it appears that the absence of atherosclerosis in the lower extremities as determined by the methods used in this investigation does not offer any assurance that the patient will not develop occlusion of the coronary arteries. Also it seems that good control of the diabetes is more effective in the prevention of circulatory disturbances of the lower extremities than in the reduction of the incidence of cardiac infarction.

The Relationship of Abnormal Cholesterol Metabolism or a High Fat Diet to Atherosclerosis

It is not our intention here to enter into any wide discussion of this controversial subject. Critical clinicians and competent experimental pathologists such as Wilder,[3] Duff,[4] Joslin,[5] Leary[6] and Weiss and Minot[7] have presented divergent yet cogent arguments either in favor of or against the view that atherosclerosis in the diabetic is caused by an abnormal cholesterol metabolism or a high fat diet. Newburgh,[8] who has always treated his patients with a high fat diet, does not believe that the incidence of vascular disease is inordinately high in his clinic. This question, it would appear, cannot be settled until a different approach can be made to the study of the development of human atherosclerosis.

Summary and Conclusions

The vascular status of 52 diabetic patients who have been under observation for a period of 10 to 13 years forms the basis of this report.

The patients were divided into three groups: Group I, those who had *excellent* or *good* care throughout most of their diabetic life; Group II, those who were regarded as uncoöperative; Group III, those who passed through the pre-insulin treatment but who had been undernourished as a result of a low caloric diet or of very severe diabetes, but who had been well controlled since insulin.

Of the patients in all groups, 23 had systolic blood pressures that were 150 mm. or more. Only six of these had diastolic blood pressures that exceeded 100. Five had systolic blood pressures that were more than 200 mm.

It was observed during this period—10 to 13 years—that there was no inordinate rise of the systolic or diastolic blood pressures in either the cooperative or uncoöperative groups. Thirty-two of the 47 patients upon whom we had blood pressure readings over a 10 year period had no essential change in their blood pressures. There was no correlation between the height of the blood pressure and the impairment of the circulation of the lower extremities.

We believe that the data presented offer further proof that atherosclerosis of the lower extremities can be prevented or delayed by controlling the diabetes continuously provided the control is started early enough after the inception of the disease. Under the conditions of this study a diet which was moderately high in fat did not produce atherosclerosis of the lower extremities provided the diabetes was kept under control. An increase of body weight appeared to favor atherosclerosis of the lower extremities but since in most instances this was associated with poor control of the diabetes it is impossible to appraise the effect of stoutness.

In the small series of patients with occlusion of the coronary arteries there was no relationship of this complication to the degree of atherosclerosis of the lower extremities as demonstrated by the methods used. It appeared that good control of the diabetes was a more influential factor in the prevention of circulatory impairment of the lower extremities than in the prevention of cardiac infarction. Coronary occlusion seemed to be favored by stoutness which was present in 15 of the 17 patients.

Eleven of the patients showed a lack of parallelism between calcification of the arteries of the lower extremities and the state of the circulation. Clinical signs of circulatory deficiency must be regarded as strong presumptive evidence of impaired circulation. Therefore it appears that the demonstration of calcification of the arteries can only be regarded as accessory evidence of atherosclerosis which may be assumed if a patient has had uncontrolled diabetes for a period. Five of our patients have had calcification of the arteries of the lower extremities for 13 years.

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OBSERVATIONS ON THE USE OF FLUIDS AND LUMBAR PUNCTURE IN THE TREATMENT OF DELIRIUM TREMENS *

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IN 1915 Steinebach,[1] reported that he observed remarkable improvement in 18 cases of delirium tremens immediately after lumbar puncture and withdrawal of cerebrospinal fluid. He thought that improvement resulted from the reduction of a high cerebrospinal pressure and a diminution of "toxic" elements circulating in the cerebrospinal fluid. Since Steinebach's first report appeared, the literature pertaining to the treatment of delirium tremens has contained other citations of the therapeutic efficacy of lumbar puncture in the treatment of this disorder (Hoppe,[2] Goldsmith,[3] and Ebaugh and Johnson [4]).

Assuming that an increase in cerebrospinal fluid pressure and edema play a significant rôle in the pathogenesis of delirium tremens, Cline and Coleman,[5] and Piker and Cohn,[6] have treated patients suffering from delirium tremens by attempting to bring about cerebral dehydration through direct and indirect means. The routine procedure of these investigators (Jr. Am. Med. Assoc., August 6, 1936 and January 3, 1937) includes the withdrawal of large quantities of cerebrospinal fluid, intravenous administration of 50 c.c. to 100 c.c. of a 50 per cent solution of dextrose, massive oral doses of magnesium sulphate and a limitation of fluid intake for the first 24 hours after admission. Improvement following this program of treatment is attributed to cerebral dehydration.

That an intravenous hypertonic solution of dextrose is productive of a significant reduction of increased cerebrospinal fluid pressure is doubtful. The immediate decrease in cerebrospinal fluid pressure which occurs after administration of an intravenous hypertonic solution of dextrose is followed within a few hours by a rise which is sometimes higher than the original level (Milles and Hurwitz,[7] Masserman,[8] Jackson et al.,[9] Lindemulder,[10] and Haug.[11]

It is common knowledge that the majority of delirium tremens patients give a history of having eaten inadequately before the onset of their delirium. During the delirium many patients perspire freely and show evidence of a general intoxication. These factors raise a question concerning the rationale of instituting intensive dehydrating measures in the treatment of uncomplicated cases of delirium tremens. Some patients appear to be dehydrated at the time of their admission to the hospital.

* Received for publication May 7, 1938.
The observations reported in this paper were made at the Boston Psychopathic Hospital Director C. Macfie Campbell.

This paper presents the results obtained in the treatment of 40 cases of delirium tremens. Twenty of the group had a lumbar puncture and were restricted in their intake of fluids. Twenty did not have a lumbar puncture and were given large quantities of fluids.

Material and Procedure

The 40 patients used in this study were men between the ages of 25 and 49 years, who were admitted to the Boston Psychopathic Hospital in 1936 and 1937. All gave a history of years of excessive drinking which was increased in amount shortly before the onset of the delirium. Upon arrival at the hospital they exhibited confusion, disorientation, visual and sometimes auditory hallucinations.

In view of the plan to give some of the patients large quantities of fluids, care was exerted to exclude from the group patients who were suspected of having intracranial conditions that are known to increase the cerebrospinal fluid pressure. Six patients had mild respiratory infections. The others were free from pulmonary complications and gross clinical evidence of liver pathology, such as jaundice and palpable hepatic enlargement. Edema was not observed in any of the cases.

No patient was permitted to have alcoholic drinks during his stay in the hospital. Immediately after admission alternate cases of the group were given an oral dose of paraldehyde sufficiently large to induce sleep. While the patient was sleeping, 10 to 40 cubic centimeters of cerebrospinal fluid were removed by means of a lumbar puncture. This procedure was followed by intravenous administration of 100 c.c. of a 50 per cent solution of dextrose. As soon as the patient awakened he was given one ounce of magnesium sulphate by mouth. Then he was allowed to have a high caloric diet rich in vitamin B and fluids amounting to 1000 c.c. for the first 24 hours. Thereafter fluids were given as the patient desired them.

The patients of the second group did not have a lumbar puncture and were not restricted in their intake of fluids. On the contrary, they were given 1500 to 2000 c.c. of a 5 per cent solution of dextrose in normal saline by hyperdomoclysis soon after admission. Later they received a high caloric diet rich in vitamin B and were urged to drink large quantities of milk, fruit juices and water. In some instances they drank as much as 2000 to 3000 c.c. of liquids within a period of 24 hours. Excitement and restlessness were controlled by oral doses of paraldehyde.

Results and Comments

All patients of both groups recovered from their delirium within one to three days after admission. However, the patients who were not restricted in the intake of fluids and did not have a lumbar puncture showed less tremulousness and fewer signs of exhaustion after the acute features of their mental disorder subsided than those patients who were treated by the lumbar

puncture and dehydrating measures. Several patients of the latter group, whom we could not keep in bed the usual length of time after the lumbar puncture, suffered from headache.

At first glance, it might seem paradoxical that in the treatment of delirium tremens two seemingly opposed procedures should induce almost equal beneficial results. Careful scrutiny of the two technics discloses, however, that both have several significant factors in common. All patients of both groups ceased drinking immediately after admission. All patients received a high caloric diet rich in vitamin B. Likewise, all patients obtained rest and sleep. It is our opinion that these factors, particularly food and sleep, played a greater rôle in recovery than might be ascribed to the effects of withdrawal of cerebrospinal fluid.

Because of reasons obvious to those who have treated excited delirium tremens patients, we were able to obtain reliable cerebrospinal fluid pressure readings in only 12 cases. All were normal. The figure is too small to enable one to draw accurate conclusions with regard to cerebrospinal fluid pressure in delirium tremens. It is significant, however, in the light of the popular belief that an increase of cerebrospinal fluid pressure exerts a conspicuous influence in the pathogenesis of this disorder.

The failure to observe an increase of cerebrospinal fluid pressure in our cases might be explained by the fact that an effort was made to exclude from the group all patients suspected of having complications which are known to initiate an increase of pressure.

Conclusions

1. Lumbar puncture is of great diagnostic significance in delirium tremens but our observations indicate that it is not an important factor in the treatment of this disorder.

2. In the absence of intracranial complications which are known to initiate an increase of cerebrospinal pressure, it seems wiser to give delirium tremens patients large quantities of fluids than to restrict their intake of fluids.

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ADVANTAGES OF PROZINSULIN* (PROTAMINE ZINC INSULIN) THERAPY: DIETARY SUGGESTIONS AND NOTES ON THE MANAGEMENT OF CASES

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Prozinsulin is being used in the routine control of the diabetic state. Difficulties have been encountered in a certain group of patients with this type of therapy. This group corresponds in part to the same group who had their difficulties with the old insulin. The purpose of this paper is to present a method, applicable in particular to the control of the unstable case. In addition, it is felt that the regime can be used with advantage in treating other diabetic patients. The successful change to Prozinsulin is dependent upon a complete rearrangement of the diet.

The physiological necessity for these suggested changes can be stated briefly.

1. Prozinsulin differs from old insulin in its delayed absorption and prolonged activity.
2. It is essential that maximal carbohydrate availability coincide with maximal insulin activity.
3. Slowly absorbed carbohydrates must be used to compensate for the delayed absorption of Prozinsulin.
4. The continuous action of Prozinsulin from supper to breakfast requires a dietary arrangement which will prevent nocturnal hypoglycemia.

The attempt to satisfy these requirements resulted in two principal changes.

1. Distribution of the amount and kind of carbohydrate, in relationship to the diurnal variations of glycosuria.
2. Insistence upon the consumption of about 30 grams of protein (150 grams of meat), or its equivalent at the evening meal.

A maximum amount of carbohydrate can be metabolized by any diabetic patient when it is distributed evenly throughout the day. When apportioned into the three customary feedings, this maximum cannot be utilized completely, and postprandial glycosuria may occur. The explanation for this lies in the fact that only so much glucose can be utilized per unit of time, and therefore, when more is presented at any one time than can be disposed of immediately, the surplus induces hyperglycemia with resultant glycosuria. In normal individuals, the self-regulating mechanisms are sufficiently elastic

* "Prozinsulin" is offered as a convenient contraction of "Protamine Zinc Insulin."

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to cope with the extreme variations of the average daily diet. The diabetic who has his insulin injected periodically, however, is limited in his diet to the predetermined COH-to-insulin ratio. Since Prozinsulin is designed to work over a long period of time, it is necessary that the COH capacity be not exceeded at any one time.

The actual amount of Prozinsulin required by any individual patient is largely a matter of trial and error. When the patient has been using old insulin, it is fairly simple to estimate the initial trial dose. This is usually two-thirds of the total daily dosage of the old insulin, given once daily, before breakfast. For the first three to seven days, supplementary doses of old insulin must be administered at breakfast and lunch-time, in five or ten unit doses. Depending upon the time and amount of glycosuria, the injections of regular insulin are stopped, first at one meal, then at both. The amount of Prozinsulin is determined by the prebreakfast urine specimen. It can be increased at three-day intervals by five-unit doses, until the morning urine specimen is sugar-free.

The patient is given a diet with the following composition: carbohydrate 150 grams, protein 80 to 100 grams, and fat in amounts required to bring the caloric intake up to the desired level. The total amount of carbohydrate is divided as follows: one-fifth for breakfast and two-fifths each for lunch and supper. The protein is divided to allow one-sixth at breakfast, and one-sixth or one-third at lunch, and two-thirds or one-half at supper. The Prozinsulin dosage is increased or decreased depending upon the morning findings in the patient's urine. When the morning urine no longer contains sugar, then changes are made in the diet arrangement to suit the conditions present. Frequently glycosuria after lunch and supper persists even though the morning urine is sugar-free. To increase the dose of Prozinsulin at this time is definitely contraindicated. The first point of attack is the post-lunch glycosuria, for, when it is eliminated, the evening glycosuria will tend to disappear spontaneously. Elimination of rapidly absorbed fruits and fruit juices, and the substitution of their glucose value by other forms of COH, is the first procedure towards solving the difficulty of post-lunch glycosuria. If this is not successful, then the shifting of five to ten grams of COH from lunch to supper should eliminate this difficulty. It is essential to spread the time of the meals throughout as much of the day as possible, in order to allow for the complete utilization of one meal before overloading with the next. In addition, this procedure will reduce the time interval between supper and breakfast. It is a common experience that hospitalized patients whose meals are served at eight A.M., eleven-thirty A.M., and four-thirty P.M., will be difficult to control with Prozinsulin. This concentration of the food within an eight hour period leads to glycosuria. The sixteen hour fasting period from supper to breakfast invites frequent hypoglycemic shocks. These very same patients, when ambulatory and treated in the diabetic clinic, present no such difficulties, in that the spacing of meals is not dependent upon such rigid hospital routine.

When the patient consumes one-half to two-thirds of the daily protein allowance at supper time, it is rare to find nocturnal hypoglycemic episodes, the reason for this being that about one-half of the protein consumed is converted into available carbohydrate. This conversion is slow. Meat is not emptied from the stomach very rapidly, and may take up to three hours.

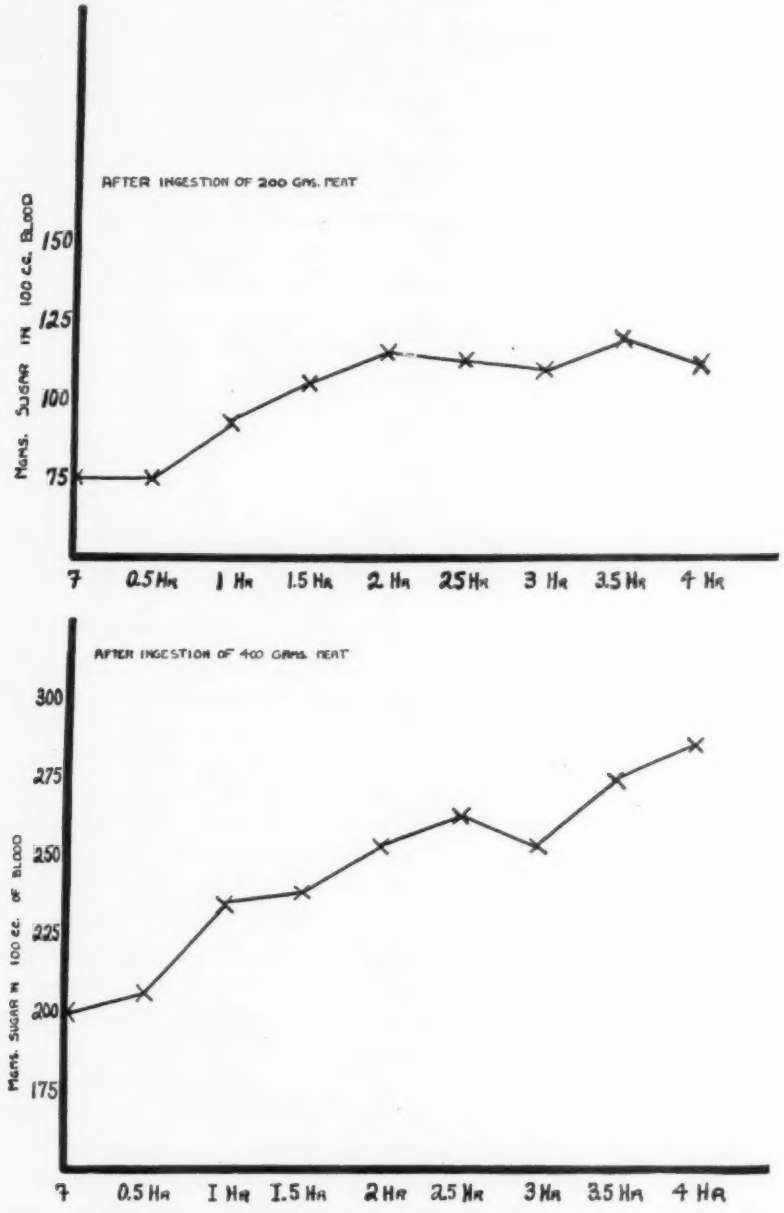

FIG. 1. The effects upon the blood sugar level of the ingestion of meat: (*a*) 200 gm. of meat, (*b*) 400 gm. of meat.

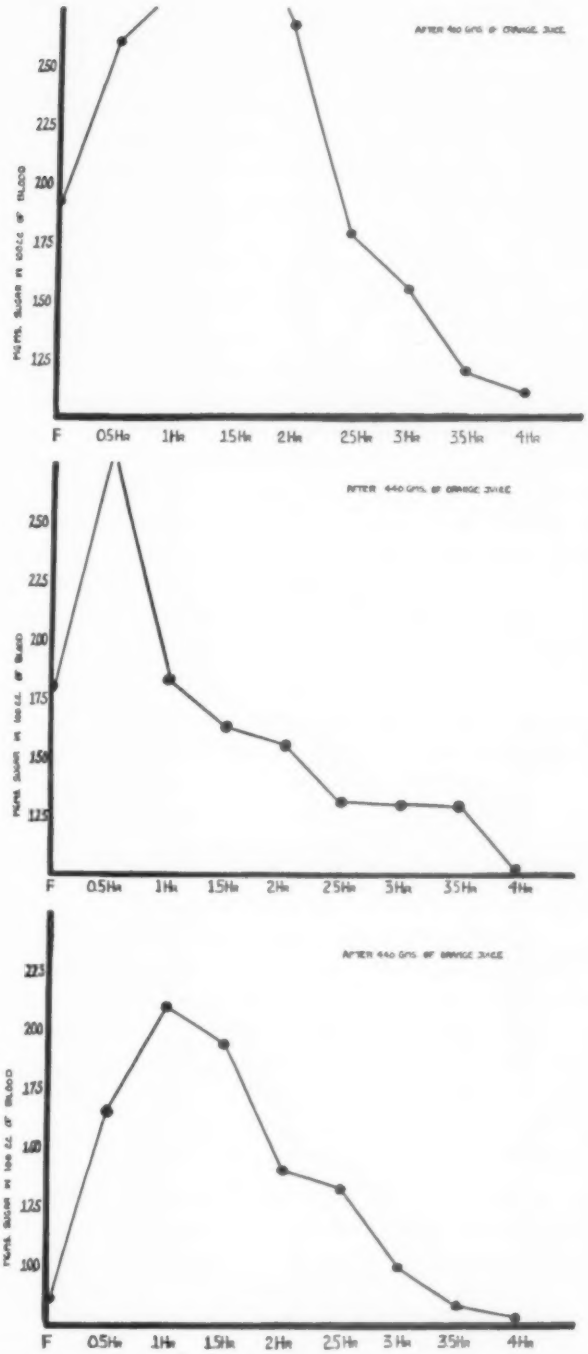

FIG. 2. Three blood sugar curves (*a*, *b*, *c*) illustrating the effect of the ingestion of 400–440 gm. of orange juice.

Then the small intestinal digestion of the meat occurs, consuming more time. The absorption of the amino acids, the de-aminization, the subsequent synthesis of the fragments to glucose, all require time. The net result is that there is prolonged availability of carbohydrate derived from the meat for six to eight hours. Experimentally, this has been shown by Conn and Newburg, and confirmed by us (figure 1, *a* and *b*). These curves represent blood sugar changes at half-hourly intervals following the ingestion of meat. No Prozinsulin was given for 24 hours preceding the test. This was done to avoid masking the slow blood sugar rise. These are examples of many similar determinations on a series of patients. These experiments were done under identically the same conditions as the orange juice experiments (see figures *2a*, *2b*, *2c*). Contrast figure 1*b* with figure *2b*. The carbohydrate equivalents were the same. The slow rise in blood sugar concentration, and the absence of any tendency to rapid fluctuations after the ingestion of meat, establishes its usefulness without question.

Some patients will require the addition of even more meat at supper and the setting of the time as late as seven-thirty to eight P.M. It is only the rare patient who actually requires a midnight feeding. Certain patients, however, request the privilege of indulging in a midnight "snack." With old insulin, this was a disturbing departure from the routine, and often necessitated an extra insulin injection at such times. With Prozinsulin, no special difficulty is encountered in allowing such liberty, provided the principle of avoiding rapidly absorbable COH is observed. Reserving part of the protein and COH from the evening meal furnishes a meat sandwich or hamburger for the midnight feeding, without causing marked fluctuations in the blood-sugar level. Prozinsulin is being used to simplify life for the diabetic, and not to complicate it. The use of multimeal schedules beyond the conventional three is an unnecessary complication.

With Prozinsulin, the commonest time for glycosuria is after breakfast. This is a natural sequence to the particular properties of Prozinsulin. The breakfast and the postbreakfast periods represent the time of minimal insulin availability. It is the period of waning activity of the previous morning's injection. The maximum availability of the current injection, by virtue of its slow absorption, does not become manifest until close to lunch time. Therefore, it is essential to prescribe the use of small breakfasts, and to eliminate rapidly absorbable fruits and fruit juices from that meal. When old insulin was administered, it was the practice to order the major fraction of the daily allowance of insulin before breakfast. Because of its rapid action, it necessitated the consumption of large breakfasts. In addition, fruits or fruit juices were a practical necessity to prevent hypoglycemia during the time before the major part of the breakfast was made available. In this series of 140 patients, very few now require the use of a single supplementary dose of regular insulin. Each patient gets along on a single dose of Prozinsulin every morning before breakfast. If postbreakfast glycosuria persists, then generally the subtraction of a few grams of COH from the

meal, as described above, eliminates this difficulty. Should hypoglycemic episodes occur consistently after any one meal, then the addition of a few grams of carbohydrate and protein to that meal is indicated. Difficulties will be encountered during the transition phase, but by the use of diet shifts these can be corrected. When the early morning urine is free of sugar the Prozinsulin dosage should not be increased without compensating by increasing the protein allowance at supper; even then, other methods should be tried first.

The hypoglycemic episodes which occur during the middle of the night and early in the morning are quite different from those which occur during the middle of the day. The nocturnal episodes, as explained above, are due to the action of the Prozinsulin long beyond the availability of the supper meal to buffer it. The daytime hypoglycemic episodes are seen more frequently in those patients having temporary postprandial glycosurias.

Figures 2, *a, b,* and *c,* illustrate the blood sugar curves of patients who had been given 400 grams of orange juice on a fasting stomach, 24 hours after the last dose of Prozinsulin. The rapid rise of the blood sugar level within one-half to one hour, and the subsequent drop to hypoglycemic levels are noteworthy. Attention should be drawn to this rapidity of the rise and fall of the blood sugar concentration. It is this precipitous drop in blood sugar concentration which initiates the subjective symptoms associated with hypoglycemia. During these tests, it was not uncommon for patients to evince symptoms of " mild shock " during the third and fourth hours. This is an illustration of the production of hypoglycemia by induced hyperglycemia; a phenomenon which is frequently observed when studying the glucose tolerance of normal people. Its occurrence in the diabetic using Prozinsulin is of more than theoretical interest, in that this mechanism can be responsible for daytime hypoglycemia. Diabetic patients using the old insulin did not show this phenomenon. As illustrated, the use of Prozinsulin brings about a sufficient restoration of COH utilization to exhibit this phenomenon, and at times even in an exaggerated form. Eliminating postprandial hyperglycemia and glycosuria practically automatically eliminates this type of hypoglycemic shock. When between meal feedings are desirable for other reasons, such as satisfying the hunger of a growing child in the mid-afternoon, then a food mixture, such as crackers and milk, or bananas and cream, is preferable to fruit or fruit juice alone. The carbohydrate of orange juice, being practically pure glucose, is rapidly absorbed and immediately available. The more complex types of carbohydrate behave differently, by virtue of the fact that the preliminary processing of digestion must take place before the monosaccharide becomes available. In addition, another method of achieving delayed availability presented itself in a method of prolonging gastric-emptying time by taking advantage of the well known effect of fats. Figures 3*a* and 3*b* illustrate the blood sugar variations in the same patients after the ingestion of the ripe whole banana, with and without cream. The effect of the addition of the cream is quite obvious. The peak rise in blood sugar

concentration is delayed until the second hour or later. The rate of rise is slower. The peak blood sugar concentration is at a lower level. The fluctuations are not as violent as without the cream. These curves were obtained 24 hours after Prozinsulin. As stated previously, the activity of the Prozinsulin becomes manifest after the second hour following the injection.

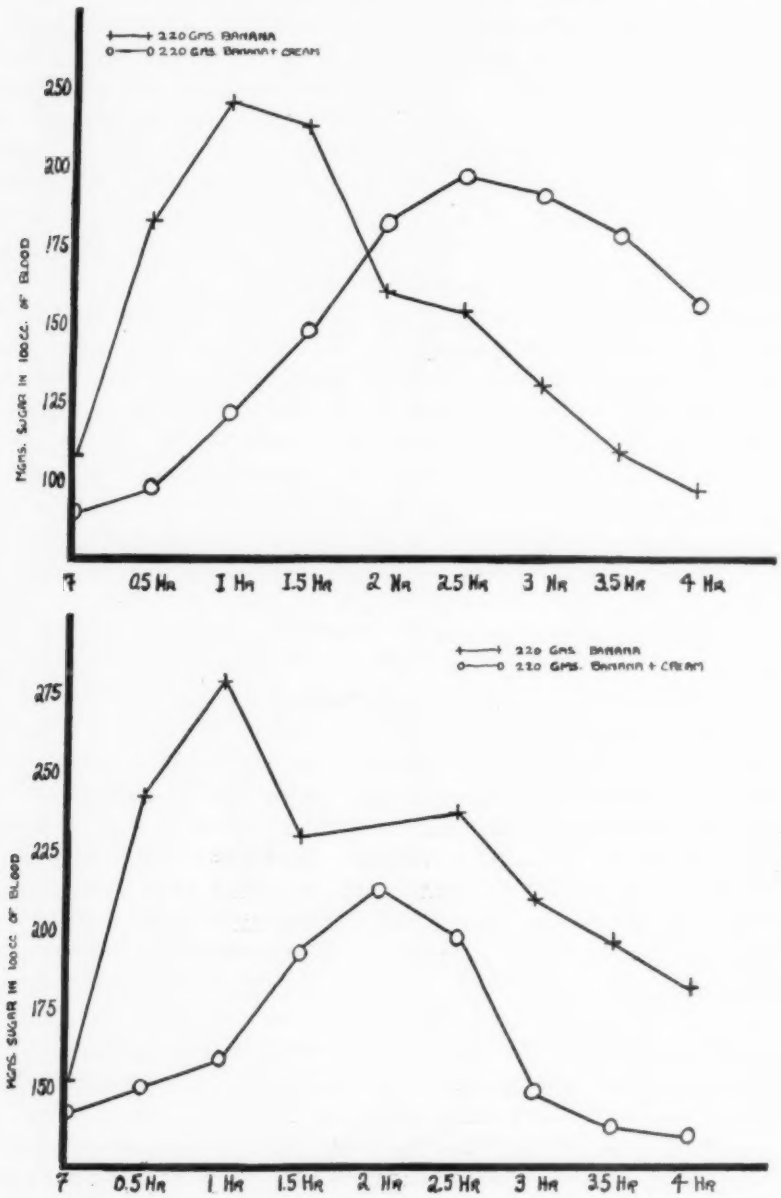

FIG. 3. Blood sugar curves in two patients (*a*, *b*) showing in each the effect of ingesting banana (220 gm.) alone and of ingesting the same amount of banana with cream.

Therefore, the use of cream with the breakfast fruit delays its availability sufficiently to bring it within the time of the beginning insulin activity of the prebreakfast injection. Experimental data are being collected as to the rate of availability of various foods and food mixtures, but the problem is so extensive that considerable investigation will be required.

A word of caution must be given to patients using Prozinsulin before indulging in unusual or very active exercise. This is one condition which must be met by extra feeding at the time of the activity, generally bread and butter. Swimming, because of the danger to life in case of hypoglycemic reaction, should always be preceded by food. One intelligent college student using Prozinsulin has determined his tolerance for golf by his score. He noticed a consistent incoördination in addressing the ball on the fourteenth tee. A bottle of popular sweet drink became standard in his golf bag, and now at the thirteenth green he drinks half of it, and has been able to compete successfully in tournaments. Another danger is skipping meals. This means that patients taking Prozinsulin cannot take the luxury of sleeping late on Sunday or any other morning, without encountering hypoglycemic episodes and their attendant dangers. Should the patient know that he is going to sleep late any one morning and skip breakfast, then he should prepare himself for it. This can be done, for example, as follows. On Saturday morning, if the patient uses over 20 units daily, he should decrease the amount of the injected Prozinsulin about 20 per cent. Late Saturday night, before going to bed, one-half of the usual Sunday morning breakfast should be consumed. With this protection, it is safe to allow the patient to sleep until his noon meal. This practice of Sunday morning breakfast-lunch is a potential danger to patients using Prozinsulin, and must be explained in detail to them.

Insofar as the technic of the actual injection of Prozinsulin goes, little need be added to what has already been described. One additional factor of safety in preventing local skin reactions has been the instruction to the patients to use five-eighths inch to three-fourths inch 25 gauge needles, and to inject as deeply as possible. It is essential to avoid intradermal injections. No detectable difference in activity exists between the U–40 and the U–80. It is preferable to inject as small a volume as is consistent with accurate measurements.

There seems to be no question about the superiority of Prozinsulin over old insulin for routine care of patients. Certainly transient and severe ketosis is less common in patients using Prozinsulin.

Table 1 summarizes the incidence of ketonuria in a group of patients before, and after the introduction of Prozinsulin in 1936. The contrast is striking and needs no further explanation.

When old insulin was used, the appearance of glycosuria was frequently associated with ketonuria. This was a result of the intermittent oxidation of carbohydrate, due to the intermittency of insulin availability. Ketonuria was especially noted in the early morning, the greatest interval of time after

TABLE I

Incidence of Ketosis in Selected Patients

Patients	1931		1932		1933		1934		1935		1936		1937	
	Total Number of Visits	Number of Visits with Ketonuria	Total Number of Visits	Number of Visits with Ketonuria	Total Number of Visits	Number of Visits with Ketonuria	Total Number of Visits	Number of Visits with Ketonuria	Total Number of Visits	Number of Visits with Ketonuria	Total Number of Visits	Number of Visits with Ketonuria	Total Number of Visits	Number of Visits with Ketonuria
J. F.....	8	5	15	13	11	8	12	10	12	9	12	0	12	0
A. J.....	30	12	40	6	20	4	16	7	14	2	40	0	40	0
G. K.....	20	9	10	2	15	2					12	0	12	0
S. M.....	9	1	12	2	10	2	12	0	12	0	12	0	12	0
M. J.....	12	4	11	1	10	4	20	2			12	0	12	0
M. B.....							16	3	14	1	35	0	35	0

the last insulin injection. Episodes of interval glycosuria may still be seen in patients using Prozinsulin, but, in spite of glycosuria of up to 10 per cent, ketosis has never been present. Because of the prolonged activity of Prozinsulin (over 24 hours) there is never any time in the course of a day when insulin is not acting. This fact is one of the strongest arguments for the use of Prozinsulin. So much so, that now it is routine to use Prozinsulin both pre- and post-operatively. In the past, patients frequently had a period of ketosis after general anesthesia, but with Prozinsulin, this can be prevented. No attempt is made to control the glycosuria completely with Prozinsulin alone. Supplementary doses of old insulin are used for that purpose. Dosage of the latter is determined by the fractional urine specimens. More satisfactory control can be achieved this way, and ketosis certainly avoided. Too much stress cannot be laid upon the necessity for complete coöperation between the surgeon and the physician, when using this therapy; properly handled, it offers definite advantages; improperly handled, it is a menace. The utmost vigilance by a properly trained nursing and house staff is required.

Time is an important factor in the treatment of diabetic coma. Old insulin is still of paramount importance in this emergency. However, there is a definite place for Prozinsulin as a supplementary agent in coma therapy. Its continuous action helps bridge the gaps between the injections of old insulin. It prevents the tendency to ketone formation in those intervals when the activity of the one injection is spent, before the next injection is given.

One of the most important contra-indications to Prozinsulin is the presence of coronary artery disease. It is felt that the complete control of the glycemia as afforded by Prozinsulin is not tolerated by the older age group

with coronary artery disease, as evidenced by increasing anginal episodes. However, if one uses Prozinsulin in comparatively small doses to prevent excessive glycosuria and ketosis, without attempting too strict a control of the diabetes, it will be tolerated. Extreme caution must be used in transferring a patient of this type from the old insulin to Prozinsulin.

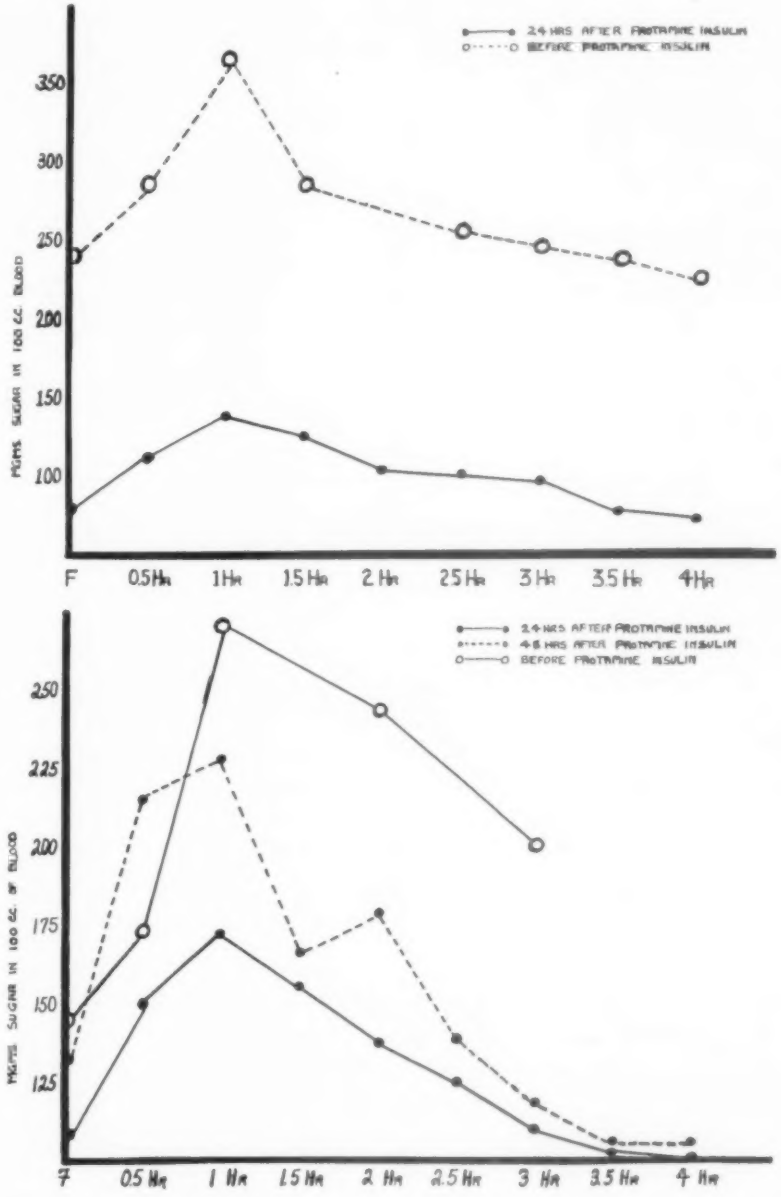

FIG. 4. Glucose tolerance curves obtained before the administration of protamine insulin and at varying intervals (24, 48 hours) after a dose of protamine insulin.

On the other hand, mild diabetics who require little or no insulin, do much better with small daily doses of Prozinsulin. The experimental data illustrated (figure 4) reveal a practically normal utilization of carbohydrate 24 hours after the injection. When no insulin is given for several days, there is a typical diabetic type of response to the test meal. If the normal glucose tolerance curve is of any significance as indicating a return to normal carbohydrate metabolism, then one can anticipate arrest, amelioration or prevention of the degenerative changes usually seen in this group of patients.

The age distribution of the patients using Prozinsulin in this clinic is given in table 2. It illustrates the general age variations in the clinic.

TABLE II

Age	Number of Cases	Age	Number of Cases
15–20	20	51–55	23
21–25	8	56–60	13
26–30	9	61–65	9
31–35	6	66–70	7
36–40	0	71–75	2
41–45	17		
46–50	16		

The patients in the older age group using this preparation are mild cases, requiring doses of 20 units or less daily. As stated previously, it is not good practice to use Prozinsulin in the severe, unstable, elderly patient, when the possibility of hypoglycemic episodes exists.

The efficiency of this insulin preparation is undoubtedly greater than that of the old insulin. Where conditions are constant, that is, diet, rate of growth, etc., the saving amounted to from 5 to 40 units daily. However, the tendency in the adolescents has been to require increased amounts as they grow in height and weight, and as the diet needs increase.

SUMMARY AND CONCLUSIONS

With proper dietary control, Prozinsulin offers definite advantages for the routine care of diabetic patients. These advantages can be stated briefly as follows:

1. The single injection daily for patients.
2. Complete elimination of transient ketonuria.
3. Closer approximation to the normal carbohydrate metabolism.
4. Decrease in the incidence of hypoglycemic episodes.
5. Valuable as a supplementary agent in coma therapy.
6. Improvement in post-operative control of diabetic patients.
7. Obviates the absolute necessity of multi-feeding schedules, yet permits optional midnight " snacks."

The essentials of the suggested dietary regimes are as follows:

1. The use of small breakfasts.
2. Division of carbohydrate into 1/5, 2/5, 2/5 for the respective morning, midday and evening meals.
3. Distribution of protein to allow for over one-half of the daily allowance at the evening meal.
4. Increased time interval between meals with particular reference to late suppers.
5. Elimination from the diet of rapidly available carbohydrate.
6. Specific use of fats in delaying gastric-emptying-time, such as cream with banana.

The majority of patients respond well, and are controlled with greater ease on such a regime. Frequent observation and meticulous attention to details of diet will be rewarded by better control of even the most unstable cases. The use of supplementary doses of old insulin can be almost completely avoided.

We express our indebtedness to Eli Lilly & Company, and to E. R. Squibb & Sons, for their generous contributions of Protamine Zinc Insulin.

CASE REPORTS

SPASM OF THE SPHINCTER OF ODDI; REPORT OF A CASE*

By Isidore Feder, M.D., *Brooklyn, N. Y.*

The sphincter of Oddi (*sphincter choledochus*) serves an important function in the regulation of the normal flow of bile from the liver into the duodenum. Recent clinical and laboratory studies have emphasized the rôle that the sphincter plays in causing pain when its normal function is disturbed. Spasm of the sphincter may produce sudden obstruction of the choledochus with a marked increase in intraductal pressure. This condition may be responsible for the initiation of attacks of severe biliary colic. Such a case is herein reported. The relevant literature is briefly reviewed.

Schwegler and Boyden [1, 2] have shown by their fine anatomical studies that the *sphincter choledochus* is a special constricting mechanism which develops at the site of junction of the common bile duct with the ampulla of Vater. The sphincter in its development is carried away from the intestinal muscle and set up as an independent mechanism for regulating the flow of bile.

Authorities differ somewhat as to the innervation of the sphincter. Doyon [3] states that the vagus contains motor fibers for the sphincter and inhibitory fibers for the gall-bladder. He observed that stimulation of the peripheral end of the splanchnic nerves caused simultaneously a contraction of the gall-bladder and an inhibition of the tonus of the sphincter. Ivy [4] feels that the vagi are the nerves predominantly concerned in increasing the resistance to the flow of bile into the duodenum and that spinal anesthesia decreases sphincteric resistance. Best and Hicken [5] state that the sphincter has an innervation derived from the sympathetic and parasympathetic systems and that it is as a rule in a contracted state under spinal anesthesia. Snell et al.[6] state that the splanchnic nerve carries sensory fibers from the bile ducts and that stimulation of this nerve causes contraction of the biliary sphincter.

The normal physiology and pharmacology of the sphincter deserve consideration. Meltzer [7] felt that the law of "contrary innervation" applied to the muscle fibers of the gall-bladder and the sphincter. During storage of bile in the gall-bladder the muscle fibers of the gall-bladder are inhibited and those of the sphincter are contracted. During discharge of bile into the duodenum the gall-bladder contracts and the sphincter relaxes. Ivy [4, 8] and Snell et al.[6] show that removal of the normal gall-bladder causes a temporary incompetence of the sphincter which later resumes its normal tone. Walters et al.,[9, 10] Colp and Doubilet,[11] Best and Hicken,[5] Snell et al.[6] and Ivy,[4, 8] by means of kymographic and choledochographic studies in the human and animal, have shown the following: Morphine and pilocarpine caused spasm of the sphincter of Oddi and an increase in intraductal pressure; nitroglycerine, amyl nitrite, atropine and intravenous bile salts relax the sphincter and decrease the resistance to the flow

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of bile into the duodenum. Meltzer [7] found that concentrated magnesium sulfate solution instilled into the duodenum through a duodenal tube caused a complete relaxation of the contracted sphincter. This observation was confirmed by Lyon and Ivy.

Abnormal function of the sphincter, without gross or microscopic anatomical changes, may cause spasm of the sphincter. Ivy [4] finds that biliary dyskinesia or dyssynergia is caused by a disordered motor state of the sphincter of Oddi. Injection of cholecystokinin will stimulate the gall-bladder to contract and in the presence of a spastic sphincter will produce biliary colic. Weir and Snell [12] feel that persistent colic after removal of the gall-bladder may be the result of physiologic obstruction to the ductal system presumably due to spasm of the sphincter. Snell et al.[6] state that spasm of the sphincter occurs mostly in women many of whom have suffered from neurogenic visceromotor disturbances. Meltzer [7] observed that psychical influences and disorganized internal secretions which disturb the emotional equilibrium may produce a tonic contraction of the sphincter and thus cause not only biliary colic but jaundice.

The symptoms of spasm of the sphincter may not differ in any marked degree from those caused by calculus in the common duct. Snell et al.[6] find that the principal symptom is a frequent occurrence of severe colicky pain in the region of the gall-bladder. Nausea and vomiting may occur but chills, fever, leukocytosis and jaundice are absent. Major attacks may be interspersed with milder seizures of a similar character. Lipschutz [13] feels that cholecystography properly conducted is the most important single procedure in the diagnosis of dyskinesia. He shows that visualization of the biliary ducts is possible when there is spasm of the sphincter. To differentiate calculus from spasm biliary drainage is of value. The presence of cholesterol crystals will point to a diagnosis of calculus.

The treatment of spasm of the sphincter is primarily a medical problem. With the gall-bladder intact a diet is given containing fats, fruit juices and meat in order to excite the gall-bladder and relax the sphincter. Frequent duodenal drainage with instillation of 25 to 33 per cent magnesium sulfate may help relax the sphincter. The drugs which have been found to be of value are the nitrites, atropine, benzedrine and intravenous bile salts. Short wave diathermy in the right upper quadrant may afford some relief. Only temporary relief is obtained from cholecystectomy for the initial relaxation of the sphincter is soon followed by a resumption of the original tone and with it renewed attacks of biliary colic. Splanchnic nerve section has been found to be valueless. Dilatation of the sphincter through the common duct is only temporary in its effect. Colp and Doubilet [14] describe an instrument called the sphincterotome which safely divides the sphincter of Oddi through the common bile duct.

Case Report

L. C., a female, 24 years of age, married, was admitted to the Beth-El Hospital on August 5, 1932. The present illness started one week prior to admission with fever, chills and malaise. There was a past history of attacks of biliary colic for 2½ years. These attacks had started shortly after delivery of her first child. Physical examination revealed rigidity of the neck, petechiae over the skin and enlargement of the spleen. A diagnosis of typhoid fever was made. All laboratory data confirmed this diagnosis. On August 20, in the fourth week of her illness, the temperature

which had begun to subside again rose and continued from then on with an intermittent character. The patient complained of severe pain in the right upper quadrant and subsequently a mass was noted in this region. The patient was operated upon September 14. An enormously distended perforated gall-bladder was found. It was completely enveloped by omentum. The gall-bladder wall at the liver site was completely destroyed and a large abscess cavity occupied the under surface of the liver. There was a calculus in the cystic duct. The gall-bladder was drained by tube and a cigarette drain was placed in Morrison's pouch. Culture of the gall-bladder pus showed the presence of *B. typhosus* and *Staphylococcus aureus*. Roentgen-ray examination showed elevation of the right cusp of the diaphragm and diminution of aeration at the base of the right lung due to the subphrenic inflammation. The temperature subsequently returned to normal. The biliary fistula continued to discharge bile and pus. The patient was discharged from the hospital November 12, 1932.

Drainage from the biliary fistula continued at home for about two months after which time the sinus tract healed. At this time the patient began to suffer attacks of biliary colic which were relieved by spontaneous opening of the sinus with a discharge of bile and pus. On May 30, 1933 the patient was admitted to the Brooklyn Jewish Hospital and reoperated upon. A thick walled, granular gall-bladder containing a bile pigment calculus, together with the fistulous tract was removed. The appendix also was removed at this time. Microscopic examination of the gall-bladder showed a fibrous, thickened serosa. The mucosa was ulcerated. The wall was infiltrated with an unusual number of plasma cells and eosinophiles. The pathological diagnosis was chronic ulcerative cholecystitis with cholelithiasis and fibrosed appendix. The patient made an uneventful recovery and was discharged June 11, 1933.

The patient felt well for about four months after her discharge from the hospital. In October 1933 she suffered a severe attack of biliary colic and from then until September 1935 had a number of these attacks with long intervals of apparently good health between the attacks.

In September 1935 an unusual sequence of symptoms began which is of the utmost interest. The patient began to have menstrual disturbances. Menstruation occurred irregularly every few weeks. Bleeding at times was only moderate and of short duration and at other times was rather profuse and lasted for 10 to 12 days. She gained about 20 pounds over a short period of time, the greatest distribution of fat being over the hips and thighs. Attacks of biliary colic began to occur more frequently. These attacks were preceded and followed by symptoms which had not existed heretofore. Previous to the onset of an attack the patient complained of extreme hunger which lasted for a few days. Then there occurred an attack of pain which started in the right upper quadrant and radiated to the back, right shoulder and arm. There was nausea but no vomiting. The height of the pain lasted a short while and was relieved either spontaneously or by morphine sulphate of which ¾ of a grain had to be given at times. Nitroglycerine in a dose of 1/50 grain given hypodermically on a number of occasions was without effect. After the attack of colic subsided there was residual tenderness in the right upper quadrant and for a number of days tenderness along the entire course of the colon. There was then a more or less abrupt cessation of pain and tenderness, at which time the patient complained of generalized itching of the skin and an urticarial rash developed. At no time was icterus noted clinically nor was there an increased icterus index during or after the attack of pain.

In December 1935, in order to reduce her rapidly accumulating weight, the patient took a number of capsules of dinitrophenol over a short period of time. This was followed by hyperpyrexia and extreme jaundice. Upon cessation of medication and after administration of intravenous glucose solution the jaundice and fever subsided.

On February 16, 1937 the patient was readmitted to the Beth-El Hospital. Blood chemistry showed albumin 4.3 and globulin 2.4 grams per 100 c.c.; sugar 86, urea 11.5,

cholesterol 110 and cholesterol ester 54 milligrams per 100 c.c. A galactose tolerance test was done on February 19. The fasting blood sugar was 87: specimens taken at ½ hour intervals for two hours after the galactose showed 95, 93, 90 and 40 mg. of sugar per 100 c.c. A glucose tolerance test was repeated February 29. The fasting blood sugar was 72; specimens taken at ½ hour intervals after the glucose showed 95, 96, 93 and 90 mg. per 100 c.c. Specimens of urine taken at the same intervals during both of these tests showed no sugar. Microscopic examination of a specimen of bile obtained by drainage did not show cholesterol crystals. The blood count, gastric analysis and Wassermann tests were negative. The basal metabolic rate was minus 22. Roentgen-ray of the gall-bladder region showed a peculiar linear shadow density about ¾ inch long in the right upper quadrant. Its cause could not be determined. Roentgen-ray of the sella turcica was negative.

In the light of the laboratory findings, the clinical symptoms were interpreted as follows: The patient was suffering from a glandular dyscrasia, in all probability hypopituitarism. This accounted for the low basal metabolic rate, the marked increase in tolerance to sugar, the gain in weight and the menstrual disturbances. Hypoglycemia was responsible for the hunger preceding the pain. The glandular imbalance led to spasm of the sphincter which initiated the attack of biliary colic.

The patient was discharged from the hospital on February 29, 1937. Glandular therapy with thyroid and pituitary extract was instituted. A rigid dietary regime was adhered to. Frequent biliary drainages were done. Short wave diathermy was given to the right upper quadrant. Despite intensive treatment the patient continued to have more frequent and very severe attacks of biliary colic. Surgical intervention was decided upon.

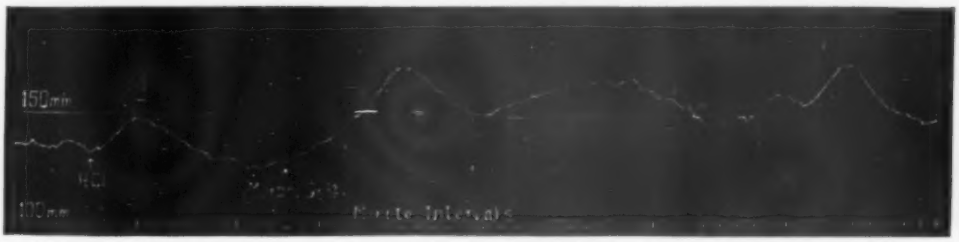

FIG. 1. Kymographic record of the resistance of the sphincter of Oddi 10 days after endocholedochal sphincterotomy.

The patient was admitted to the Mt. Sinai Hospital on March 25, 1937. She was operated upon on March 26 by Dr. Ralph Colp. The liver and gall-bladder bed appeared normal. The common duct did not appear dilated and was found to contain golden yellow bile. There was no obstruction upwards toward either hepatic duct and a probe could readily be passed into the duodenum. The pancreas showed no adenomata. No common duct stones could be felt, but on the posterior wall of the pancreas there could be felt a narrow, hard ridge running at right angles to the pancreatic duct. The nature of this ridge was difficult to determine (this accounted for the peculiar linear shadow density seen on the previous roentgen-ray). The sphincterotome was inserted into the common duct and down into the duodenum and the sphincter of Oddi was cut and a section of it removed.

A "T" tube was inserted into the common duct. The patient made an uneventful recovery. Figure 1 is a kymographic record of the resistance of the sphincter of Oddi ten days after endocholedochal sphincterotomy. The resistance was found to measure 130 mm. of water. Following intraduodenal instillation of dilute HCl, the resistance rose to 145 mm. falling to the original level in ten minutes. The hypodermic injection of morphine caused the resistance to rise to 145 mm. at which level it remained for the duration of the experiment.

Figure 2 is a typical kymographic tracing in a patient in whom the sphincter had been left intact. The original resistance (160 mm. of water) rose to 255 mm. follow-

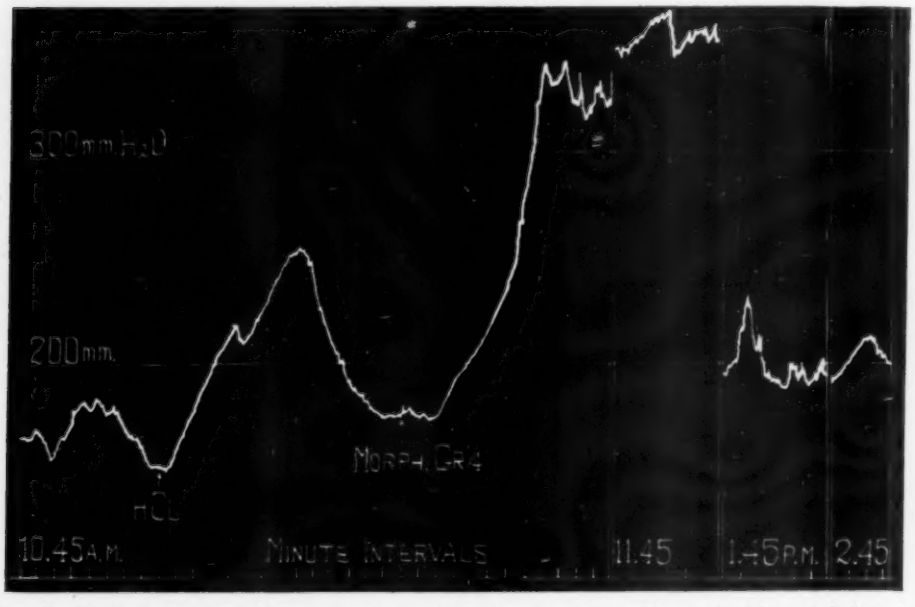

FIG. 2. Typical kymographic tracing in a patient in whom the sphincter had been left intact.

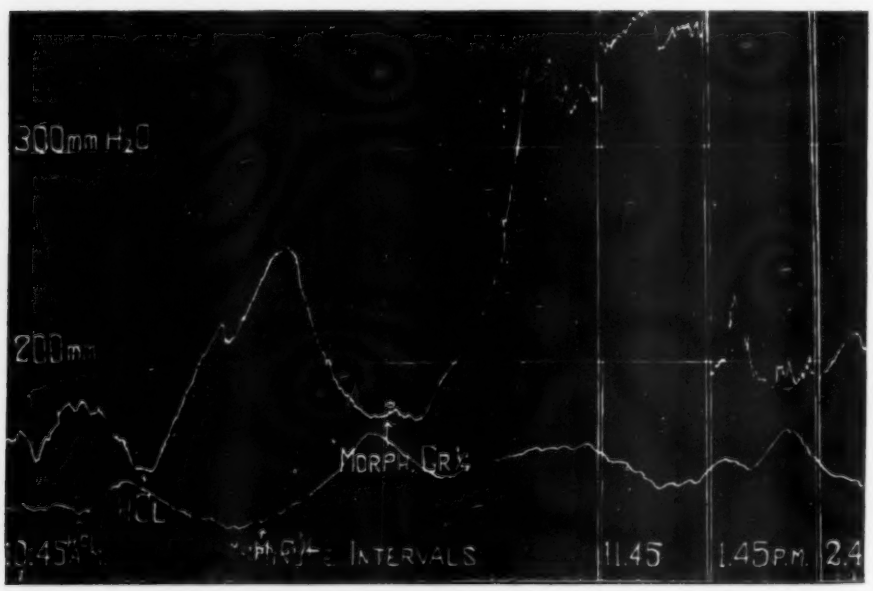

FIG. 3. The tracing from the patient in whom the sphincter of Oddi was sectioned (figure 1) superimposed upon the tracing in a patient with an intact sphincter (figure 2). The difference in the levels of the tracings clearly shows the small part played by the duodenal musculature and the important part played by the sphincter of Oddi.

ing the local application of dilute HCl. The spasm produced by morphine raised the resistance to 370 mm. of water.

Figure 3 shows the tracing from the patient in whom the sphincter of Oddi was sectioned (figure 1) superimposed upon the tracing in a patient with an intact

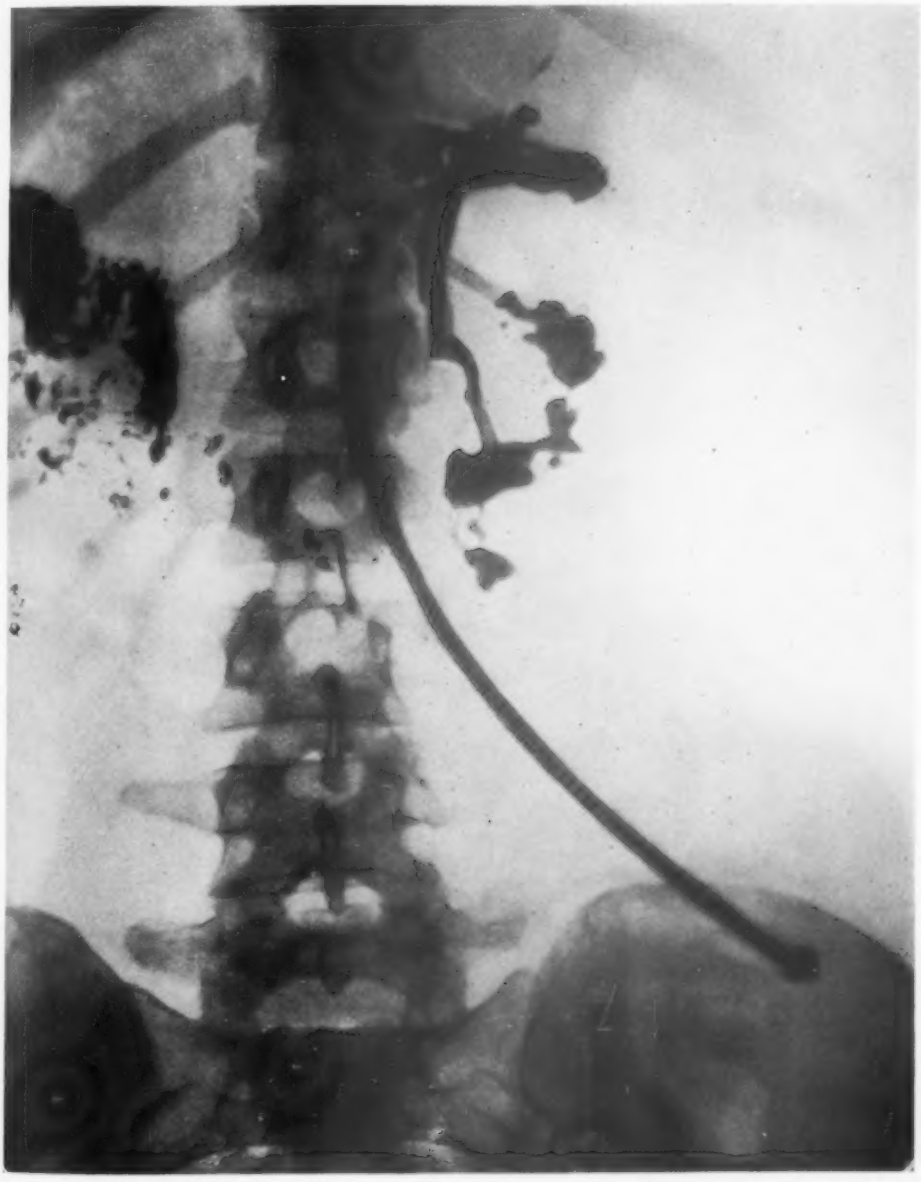

FIG. 4. Lipiodol study 11 days after sphincterotomy before administration of morphine.

sphincter (figure 2). The difference in the levels of the tracings clearly shows the small part played by the duodenal musculature and the important part played by the sphincter of Oddi.

Figures 4 and 5 show lipiodol study 11 days after sphincterotomy. The resistance of the common duct sphincter was so low (figure 4) that the terminal portions of the

FIG. 5. Lipiodol study in case of sectioned sphincter of Oddi after administration of morphine.

hepatic ducts and the upper end of the choledochus were not outlined before lipiodol entered the duodenum. Following the administration of morphine (figure 5) the duodenal wall was seen to become spastic, compressing the intramural portion of the

choledochus. The resultant increase in the resistance was slight, since only the terminal portion of the hepatic ducts was visualized before lipiodol entered the duodenum. These studies confirm the results of the kymographic tracing (figure 1).

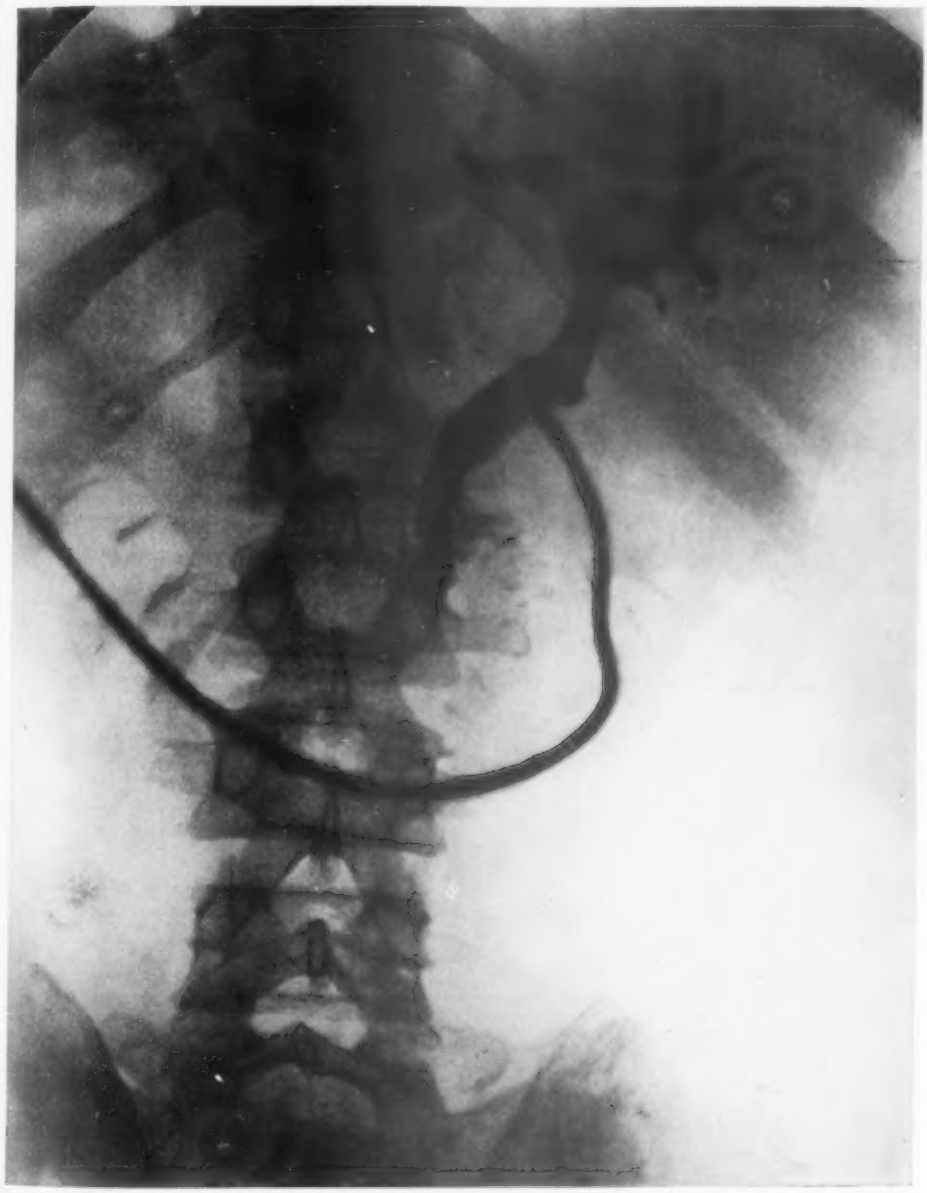

FIG. 6. Lipiodol study in patient whose sphincter was left intact before administration of morphine.

Figure 6 shows lipiodol studies before and figure 7 after the administration in the patient whose kymographic tracing is recorded in figure 2. Note that in figure 4 (manometric resistance 165 mm.) and in figure 6 (manometric resistance 160 mm.)

the terminal ends of the hepatic ducts are visualized to an equal extent. The spasm produced by morphine in the intact sphincter of Oddi (figure 7) raised the resistance to such a height (370 mm.) that the very fine biliary radicles were visualized before lipiodol entered the duodenum.

FIG. 7. Lipiodol study in patient whose sphincter was left intact after administration of morphine.

The patient was discharged from the hospital April 1937. She has been on a full diet without any medication. There have not been any attacks of biliary colic during the past year. There have been, however, episodes of hunger followed by generalized urticaria. The etiologic factor in this case, i.e. the glandular dyscrasia, still remains. The attacks of biliary colic have been avoided by sectioning the sphincter of Oddi. This procedure has made improbable the recurrence of spasm of the sphincter with its resultant increase in intraductal pressure.

Summary

The subject of spasm of the sphincter of Oddi has been briefly reviewed.

A case presenting a train of symptoms typical of this condition is reported.

A glandular dyscrasia appears to have been the etiologic factor in this case.

Cessation of the attacks of biliary colic has been obtained by surgical section of the sphincter of Oddi.

Roentgen and kymographic evidence is presented to show that an appreciable rise in intraductal pressure cannot be obtained in the presence of a sectioned sphincter of Oddi.

I wish to express my sincere appreciation to Dr. R. Colp and Dr. H. Doubilet for their kindness in presenting me with the excellent photographs which illustrate this paper.

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SYSTEMIC POISONING DUE TO SYNTHETIC ORGANIC HAIR DYE: FATAL CASE WITH AUTOPSY*

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HAIR dyeing, a practice of great antiquity, is still widely prevalent today. A variety of materials are used for the purpose of producing variously tinted hair. These substances fall into three groups: (1) Those of vegetable origin (henna, chamomile); (2) metallic substances (silver, manganese, bismuth); (3) synthetic compounds (paraphenylenediamine, paratoluylenediamine, pyrogallol). Because of the ease of application, the relative permanence, and supposed "naturalness" of the resulting tints, the last group has been greatly exploited in recent years. Soon after their introduction, however, as important fixtures in the cosmetic armamentarium, reports of toxic effects began to appear in medical literature.

Because of these adverse comments and of restrictive legislation adopted in some European countries and in certain states in this country,[1] it has been necessary for the manufacturers to change the composition of their products on several occasions. Paraphenylenediamine was the first of the synthetic compounds to be used and is still, probably, widely used even today. In the hair dye under consideration, this substance was replaced by paratoluylenediamine, a supposedly non-toxic agent. That the changed product was entirely innocuous was, however, belied by further reports of toxic manifestations. As a result, if the product was to continue to be marketed commercially, another change was necessary.[2] The most recent chemical substitute to be used is reported to be pyrogallol.

Medical literature abounds in descriptions of local dermatologic mishaps following the use of synthetic hair dye, usually paraphenylenediamine, but a careful review of the literature reveals reports of but few cases of systemic poisoning, and only one of these reports contains necropsy data.[1,2] It is our purpose to record a second fatal case with necropsy findings.

Since we are concerned with a hair dye which at one time or another has contained paraphenylenediamine, paratoluylenediamine and pyrogallol, it may not be amiss to briefly consider some properties of these agents. Paraphenylenediamine, $C_6H_4(NH_2)2$, was first prepared by Hoffman in 1854.[3] In actual practice this substance when combined with hydrogen peroxide forms a product known as quinone di-imine (Bandrowski's base) which is believed to be the actual tinting agent. Hanzlik[4] has studied the pharmacologic effects of the phenylenediamines on rabbits. These are characterized by stimulation of the circulation and respiration, fall in body temperature, tremors, increased reflex excitability, convulsions, coma and death. The hypodermic or gastric administration of paraphenylenediamine has been noted furthermore to produce edema of the face, nose, conjunctivae and neck. This substance, under the trade name of ursol, is used to dye furs and has been known to produce dermatitides about the neck of wearers.[5] As a purely industrial hazard, it has long been known

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to lead to asthmatic-like attacks in fur workers [6] and is, moreover, a toxic hazard in the rubber industry where it is used as an accelerator of the process of vulcanization.[7] The toxic effects, noted in profusion in medical literature in the early years of this century were chiefly of a local dermatological nature.[8] The further use of this compound to dye the eyelashes was followed by various ophthalmic complications ranging from conjunctivitis to corneal necrosis and even death.[9] Cases of systemic poisoning have been reported by Nott,[10] Close,[11] and Israels and Susman.[12] The former, in 1924, cited a case which was characterized by an acute onset, marked cyanosis and prostration. These symptoms bore a marked resemblance to those produced by acute aniline poisoning. In 1932 Close reported a case with symptomatology of a neurological and gastrointestinal nature. The manifestations included nystagmus, tinnitus, giddiness, headache, flatulence and anorexia. Recovery followed shaving of the head of the patient.

Of considerably more interest is the first recorded fatal case reported by Israels and Susman in 1934. Their patient, a young woman, who worked as a dyer in a hairdressing establishment, complained of jaundice, weakness, headache, sore-throat and joint pains. Slight hepatomegaly was present on examination. The Van den Bergh reaction was of the prompt direct positive type. Other laboratory data revealed a moderate anemia, slight leukopenia and diminution in platelets. No accurate data concerning red cell size were given. The patient's course, under observation, was rapidly downhill and was marked by steadily increasing jaundice. Postmortem examination revealed a coarsely nodular liver somewhat diminished in size, ascites, moderate splenomegaly and scattered purpuric hemorrhages on the skin and gastric mucosa. On microscopic examination of the liver the authors found what they termed "typical features of subacute yellow atrophy."

As a corollary to the liver damage which appears as the outstanding pathological finding in the above case and in the one to be presented, it is of interest to note the three cases reported by Baldridge [13] in 1935. He found in these patients macrocytic anemias with aplastic features, associated with the periodic application of synthetic organic hair dyes. In two cases the active dyeing agent was reported as paraphenylenediamine and in the other toluylenediamine. Two had definite macrocytosis by volume index and all showed varying degrees of anemia, leukopenia and thrombocytopenia. Liver function tests were not reported, nor was any mention made of jaundice. Improvement apparently followed cessation of dyeing. No explanation beyond possible idiosyncrasy is offered by Baldridge for these occurrences. The rôle of liver damage in the causation, at times of macrocytic anemia has been stressed in the last few years.[14] It is commonly stated that there is a failure by the liver in such cases to properly store or utilize the anti-anemic factor of Castle. This simple explanation, it is true, is objected to by some authorities including Minot,[15] but the fact remains that, whatever the mechanism, it is the experience of all that liver damage carries with it a definite incidence of macrocytic anemia. The macrocytosis, moreover, may be a transient one depending on such transient hepatic damage as occurs in so-called catarrhal jaundice and chronic passive congestion.[16] It would seem to us, then, in the light of the above facts and the demonstrated liver lesions in Israels and Susman's case and in the present one that there is at hand a ready

explanation of the macrocytosis observed by Baldridge. This evidence of dyshemopoiesis was a prominent feature of the case to be presented.

Toluylenediamine, $C_6H_3(NH_2)2$, a closely allied chemical product, was used over a period of years as a substitute for paraphenylenediamine. The pharmacological activities of this agent have been known for many years. It will produce marked jaundice in experimental animals. The mode of production has been disputed, some observers asserting it to be of a hemolytic nature, while others claim it to be the result of toxic liver damage. Wolff [17] has recently demonstrated that apparently the latter view is correct, i.e. there is actual hepatic parenchymal damage in the nature of a toxic hepatitis.

Pyrogallol, $C_6H_3(OH)_3$, the most recent dyeing constituent, is potentially a toxic hazard. Sollman [18] states that it may produce an intense acute nephritis, form methemoglobin and cause hemolysis of red blood cells. We are not aware of reports of deleterious effects, specifically attributable to this product when used as a hair dye.

With this brief survey of the grimmer aspects of hair dyeing we wish to record a case of toxic cirrhosis of the liver, terminating fatally and subsequently necropsied, in which there was a history of repeated, long-continued application of synthetic organic hair dye.

Case Report

M. O'S. a white female, aged 61, a practical nurse by occupation, was admitted to the medical service of Dr. M. C. Pincoffs at Mercy Hospital on September 6, 1935. The presenting complaints were "weakness and abdominal swelling of several weeks' duration." Her illness dated back nine months to January 1935, when, as was later ascertained, she had had her hair dyed with a synthetic organic dye and just subsequent to its application had received a permanent wave. This was the last time the hair dyeing procedure was carried out, but it was ascertained that she had been accustomed to have her hair dyed on an average of every two months over a period of 15 years and had continuously used the same product. The coincidence of the permanent wave with the dyeing procedure was believed to have occurred only this time. Soon after, during January, she experienced attacks of epistaxis which seemed to occur in association with excitement. The occurrence of a domestic tragedy at this time produced a "nervous breakdown" to which was attributed many symptoms which ensued. These included ready fatigability and episodes of dull aching pain over the precordium and in the left lower quadrant of the abdomen. Early in July 1935, she first became aware of a mass in the left upper abdomen, and mild edema of the ankles appeared at this time. On the advice of a physician the patient spent five weeks in bed with resultant disappearance of the edema. Late in August an attack of diarrhea associated with melena occurred and lasted about two days. Hospitalization was advised soon after.

Further questioning revealed a history of anorexia, constipation of 3 to 4 years' duration, abdominal distention of several weeks' duration and loss of 20 pounds in weight during the nine months of illness. Exertional dyspnea had been noted during the year preceding admission and edema of the ankles for two months. Nocturia, two to three times, was present.

The family history was entirely non-contributory. An attack of typhoid fever had occurred about 1905. A history of several so-called gall-bladder attacks associated with jaundice was elicited, but the exact dates could not be ascertained. Menopause had occurred six years before, but an episode of vaginal bleeding of three days' duration was present one year later.

Examination, on admission, revealed an elderly, somewhat obese, white female, who was lying quietly in bed. Graying of the roots of the hair merging into a brownish color at the free ends was noted. There was complete adentia. The papillae of the tongue were present. Examination of the heart and lungs was essentially negative. The blood pressure was 106 systolic and 60 diastolic. The abdomen was obese and symmetrically distended. Tenderness was elicited on pressure in the right upper quadrant of the abdomen. In the left upper quadrant a mass, identified as spleen, was noted extending to the midline and from the costal margin to the level of the umbilicus. Several ecchymotic patches were noted on the right leg and one on the left. The reflexes were normal and no pathological reflexes could be obtained.

Pelvic examination revealed no abnormality. Inspection of the fundi revealed a few scattered, whitish, retinal spots, which were believed by the ophthalmologist to be congenital in origin.

A number of roentgen-ray studies were made including a gastrointestinal series, pyelograms and films of the long bones and chest. The abdominal roentgenograms revealed the presence of an extra visceral mass (spleen) in the left upper quadrant causing a pressure deformity of the stomach and interfering with the emptying of the left renal pelvis. The other films were completely negative.

The comprehensive laboratory studies can be summarized as follows: Repeated urinalyses were negative except for the appearance of urobilin terminally. Blood chemical determinations showed normal values for sugar and urea throughout. The Van den Bergh reaction was prompt, direct, positive. The blood bilirubin rose from 0.625 mg. to 30 mg. terminally. The bromsulphalein test of liver function revealed 20 per cent retention of dye at the end of two hours. Blood Kolmer and Kahn tests were negative. Aside from the presence of occult blood on several occasions, stool examinations were also essentially negative. Gastric analysis revealed normal values for both free and total acid.

The hemocytological picture on admission was as follows: Hemoglobin, 74 per cent (12.2 gm. Sahli); red blood cells, 3,840,000; white blood cells 2,250. The differential count showed: Polymorphonuclear neutrophiles, 76 per cent (6 per cent staff forms); lymphocytes 19 per cent; monocytes 6 per cent. Further blood pictures during the course in hospital revealed a steady diminution in hemoglobin, red and white blood cells. The latter, however, increased terminally to 10,250 under the influence of a localized septic infection.

The bleeding time was three minutes and the coagulation time five minutes. A fragility test revealed incipient hemolysis in saline solution at 0.35 per cent and complete hemolysis at 0.25 per cent. Platelet counts varied from 38,500 to 65,400 (Olef technic; normal, 500,000) and the Rumpel-Leede phenomenon was positive. A Price-Jones graph revealed definite widening of the base and a distinct shift to the right. The mean corpuscular volume was 114 cu. microns and the volume index 1.2. Reticulocyte counts varied from 2.2 per cent to 7 per cent, the latter being obtained seven days after the institution of adequate intramuscular liver therapy. Sternal bone marrow, obtained by the puncture method, revealed slight normoblastic increase as well as increase in percentage of lymphocytes, but no other deviations from normal.

The patient's stay in the hospital totalled 55 days and during the first four weeks of this period her temperature, pulse and respirations remained within normal limits. She became somewhat irrational about three weeks after admission, apparently coincidentally with an increase in jaundice. Three attacks of epistaxis of moderate severity occurred about one month after admission. Neurological reexamination, several weeks after entrance to the hospital, revealed impairment of proprioceptive sensation and apparent loss of vibratory sensation below the third lumbar vertebra. On October 20, five weeks after admission, an abscess of the left buttock, at the site of an intramuscular injection of liver, was noted. This required incision and drainage and was associated with a septic temperature which continued

until death. Liver therapy, as has been stated, produced some reticulocytosis, but no specific increase in red cell count. The patient was treated symptomatically with daily intravenous glucose injections, but steadily became more toxic and irrational. Pitting edema of the lower extremities and distention of abdomen were pronounced terminally. The patient gradually lapsed into coma and died November 1, 1935, approximately eleven months after the onset of symptoms.

Autopsy

Necropsy was performed eight hours after death. The following report is abbreviated, but no pertinent data are omitted. The external examination revealed an elderly, obese, white female, who was markedly jaundiced. The hair of the scalp displayed a variegated appearance with that portion closest to the roots being gray and the free ends of a reddish-brown color. The abdomen was quite distended.

The peritoneal cavity contained 2,000 c.c. of clear, yellow, serous fluid. The spleen was enlarged and extended five cm. below the left costal margin. The liver appeared small and was tucked up beneath the right costal margin. The pleural cavities displayed no changes of significance aside from the presence of a few fibrous pleural adhesions at the left apex.

The heart was of normal size and displayed no unusual gross changes beyond yellowish discoloration of the mural and valvular endocardium whose appearance was shared by other serous surfaces. Slight atherosclerotic changes were evident in the aorta. Hypostatic changes were seen in both lungs macroscopically.

The liver weighed 1150 gm. Its external surface was of a coarse, diffusely nodular appearance. These nodules varied in size from three mm. to one cm. and were brownish-green in color. The intervening depressions were gray-brown. The capsule appeared somewhat thickened, but translucent (figure 1). Increased resistance was met with on sectioning. The cut surface revealed complete distortion of the normal architecture, due to diffuse nodulation. These deep nodules were of similar appearance to those of the capsular surface. The gall-bladder and biliary passages were devoid of gross lesions.

The spleen weighed 700 gm. It was of normal consistency and presented a smooth, glistening, taut capsule. The cut surface was of a dark, wine-red color and the Malpighian bodies were obscure.

The entire genito-urinary apparatus was free of any noteworthy change. Examination of the gastrointestinal tract likewise revealed no gross pathologic lesion. The adrenals, macroscopically, were normal.

Permission to examine the brain and spinal cord was not obtained.

The important histopathological changes were noted in the liver and spleen. In addition, a terminal lobular hypostatic pneumonia was present in the lower lobes of both lungs. The presence of bile pigment was noted in the tubular epithelium of the kidney and in the adrenal cortex.

Sections of the liver showed marked distortion of the normal architecture, due to the presence of broad, anastomosing bands of dense, but cellular connective tissue which completely destroyed the preëxisting lobular arrangements (figure 2). The remaining groups of parenchymal cells displayed various degenerative and necrobiotic changes (figure 3). Numerous large, fat vacuoles were seen in many cells. Others were edematous and showed granular cytoplasmic changes with resultant marked sinusoidal narrowing. Still others had progressed to complete necrosis, with pyknotic, karyorrhectic and karyolytic nuclear changes. Many cells displayed marked bile pigmentation. The intervening fibrous tissue was the seat of a diffuse lymphocytic invasion and displayed the presence of numerous abortive bile canaliculi and thin-walled blood spaces. The extensive fibrosis suggested obliteration of whole lobules of liver parenchyma.

FIG. 1. Liver is diminished in size and presents a coarsely nodular surface.

Sections of the spleen revealed a normally cellular and distinctly congested pulp with the reticulum and sinuses sharing the latter. Occasional clumps of brownish-green pigment were observed within reticular cells. The Malpighian bodies were of normal histological structure.

The anatomical diagnosis may be stated as follows: Subacute yellow atrophy of the liver; chronic passive congestion of the spleen (splenomegaly) and gastrointestinal tract; ascites (2,000 c.c.); jaundice, severe; lobular pneumonia, bases, bilateral.

COMMENT

The etiological concepts of toxic cirrhosis or healed yellow atrophy have been considerably broadened since the relationship between this fibrotic stage and an earlier necrotic process was established by Mallory.[19] Many inorganic and organic chemicals entering the body by a variety of routes such as ingestion, inhalation and injection are known to produce severe hepatic parenchymal damage. The more commonly known of these include phosphorus, arsphenamine, chloroform, cinchophen, carbon tetrachloride and phenylhydrazine. In this in-

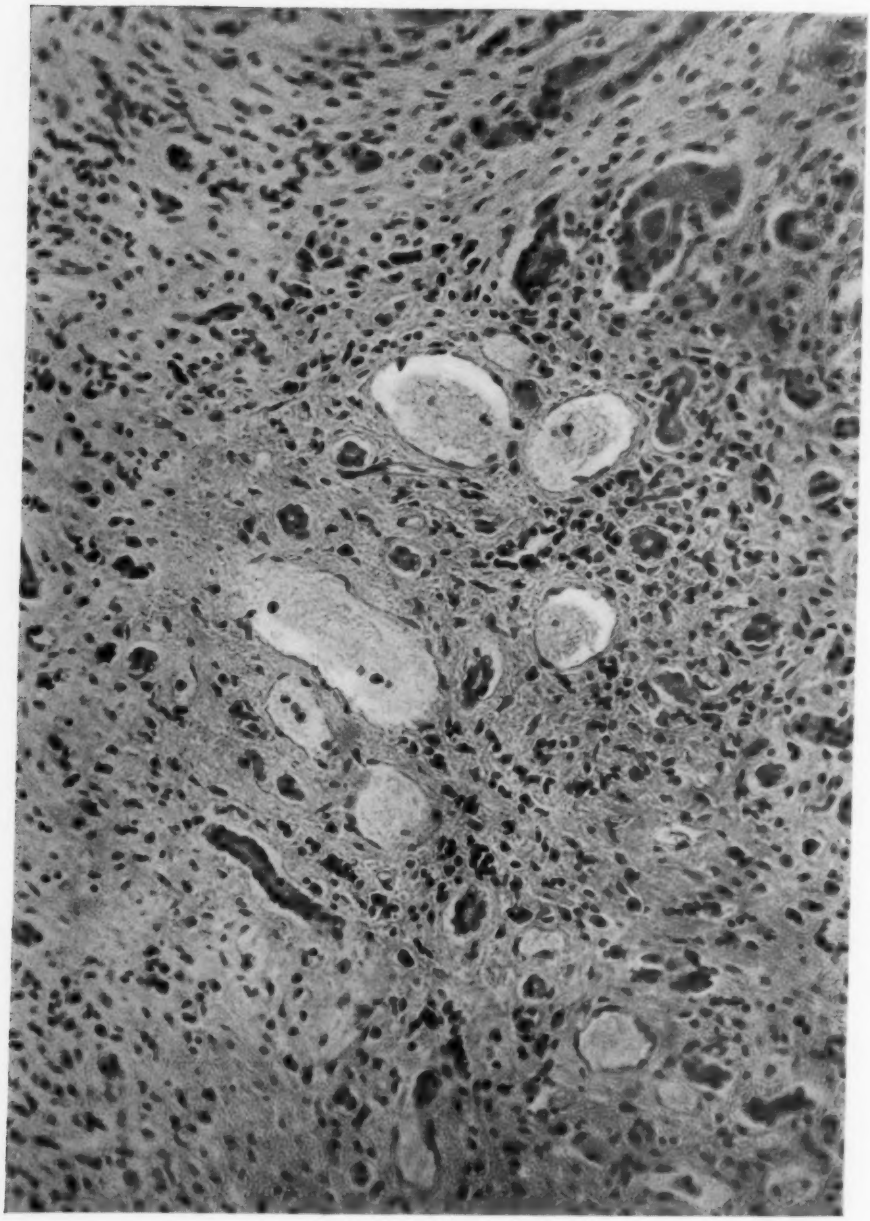

FIG. 2. Liver. Distortion of architecture by broad anastomosing bands of fibrous tissue. Note lymphocytic infiltration, presence of numerous dilated vascular spaces and proliferating bile canaliculi. × 100.

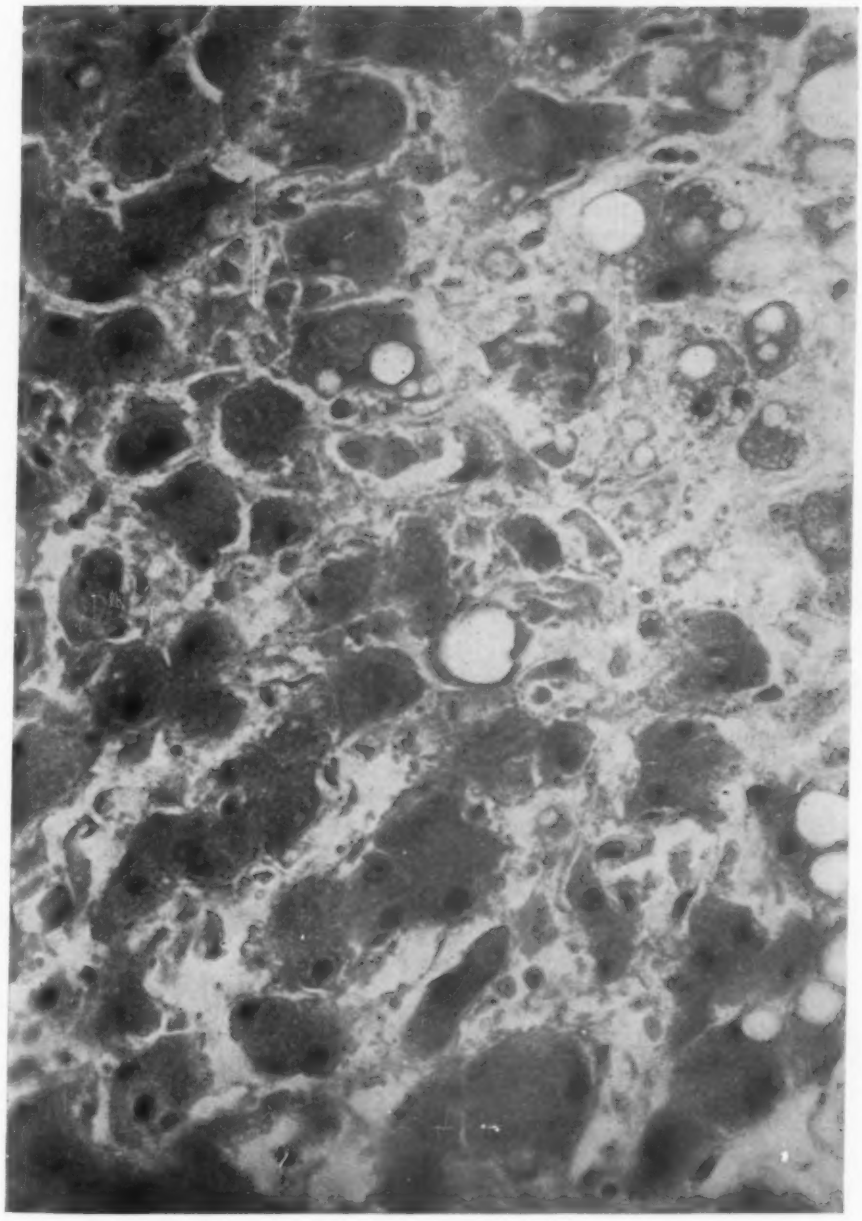

FIG. 3. Liver. Note fat vacuolization and necrobiotic changes in remaining parenchyma.

dustrial era the possibility of contact with many, as yet unknown, hepatotoxins increases immensely. Paratoluylenediamine has long been known to produce severe jaundice, the pathogenesis of which has been recently shown to be due to liver parenchymal damage. The use of this substance had apparently been largely confined to experimental procedures until it was found to be commercially useful as a hair dye. The first necropsied fatal case of hair dye poisoning in 1934 revealed marked liver damage. This was attributed to paraphenylenediamine by the authors who stated that theirs was the first recorded instance of hepatic injury. Their report does not include any data concerning the actual commercial preparation used. Because of the widespread use of paraphenylenediamine, both as a cosmetic and in industry, this rarity of liver damage is difficult to explain. Moreover, pharmacological studies of the toxic effects of the phenylenediamines reveal no evidence of liver damage. It appears quite probable, to us, that a commercial hair dye of secret and changing composition could have contained paratoluylenediamine, a known hepato-toxin, at the time this fatality was recorded. The report of Baldridge likewise fails to reveal any careful correlation between the dyeing constituents and the macrocytosis which he observed.

A careful consideration of the literature of hair dye poisoning reveals the fact that dermatological complications occurred in profusion during a time when paraphenylenediamine was widely used. The two autopsied fatal cases (including the present report) occurred during a time when exposure to paratoluylenediamine was possible.

To recapitulate briefly then, we may state that the demonstration of paratoluylenediamine as an experimental hepatotoxic substance, the occurrence of two necropsy proved cases of severe liver damage in patients exposed to its effects in a hair dye, the absence of any other known etiological factor in these patients, and the citation of three cases of atypical macrocytic anemia in persons using the dye appear to offer some tenable evidence for regarding the association of the two factors of hair dyeing and liver pathology as more than mere coincidence.

The incidence of liver damage in persons who have been exposed to this chemical agent is extremely difficult to ascertain. It would seem that it is somewhat infrequent. The toxic action may be on the basis of personal idiosyncrasy such as is exhibited to so many other coal-tar derivatives. It has been suggested by Baldridge that the heat and ammonia used during the application of a "permanent wave" may have aided in the rapid absorption of the dye and the onset of symptoms in his cases. It is notable that the coincidence of these two procedures occurred in our case just prior to the onset of symptoms. The limited data offered by the two necropsied cases do not permit of wide generalizations, but offer an interesting avenue of inquiry in cases of jaundice of obscure etiology in females.

Summary

1. Toxic effects from synthetic hair dyes have been frequently reported in medical literature. Most have been of a local dermatological nature. Several cases of systemic poisoning have been noted in the literature, only one of which resulted fatally and was necropsied.

2. The synthetic group of dyes includes those frequently used today. Among

these are paraphenylenediamine, paratoluylenediamine and pyrogallol. Paratoluylenediamine is a known hepatotoxin.

3. A case is reported of prolonged use of a synthetic hair dye followed by a fatal illness which was characterized clinically by severe jaundice, splenomegaly, macrocytic anemia and beginning postero-lateral cord changes. Pathological, toxic cirrhosis of the liver was the outstanding feature. This is apparently the second necropsied case in medical literature.

4. Evidence supporting the relationship between the use of synthetic organic hair dyes and liver damage is offered.

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EDITORIAL

FURTHER ADVANCES IN THE TREATMENT OF PELLAGRA AND ASSOCIATED DEFICIENCY DISEASES

In an editorial in the March 1938 number of the ANNALS we pointed out the relatively unsatisfactory results obtained by the usual methods of treating pellagra and discussed the striking improvement noted in the earliest reports regarding the administration of nicotinic acid to patients with this disease. During the year and more that has since elapsed, a large number of patients with pellagra have been treated with nicotinic acid by many different observers, and in general the successful results reported in the early experiments have been amply confirmed. Even if the patients are kept on the deficient pellagra-producing diet, the administration of nicotinic acid brings about an abrupt, dramatic improvement. This is shown particularly in the prompt subsidence of the stomatitis and of the inflammatory changes in the other mucous membranes, in relief from the general malaise, anorexia and digestive disturbances and in the disappearance of the mental confusion and the psychoses, at least in the early acute stages. The cutaneous lesions proved relatively resistant, although the erythema also disappears.

These observations, however, have also confirmed the clinical impression previously held by many that pellagra as it occurs naturally is a multiple deficiency disease and cannot be attributed entirely to a lack of any one single substance. If patients with pellagra are kept on the deficient diet but given adequate quantities of nicotinic acid, in many cases there is a persistence or a recurrence of certain disease symptoms. The most frequent and prominent are numbness, paresthesias, pains and even paralyses which are manifestations of a peripheral neuritis. These are especially marked in alcoholic addicts, but are common among endemic cases also. It has been shown, especially by Spies and his associates,[1] and by others also, that they are manifestations of an associated beriberi and can be cured by the administration of crystalline vitamin B_1.

The administration of both thiamin and nicotinic acid does not restore to normal health an individual kept on such a restricted diet. Various symptoms may persist or eventually appear which, in large part at least, are attributable to riboflavin deficiency. This vitamin was the first to be isolated and identified from the old vitamin B_2 complex. Its structural formula is known and it has been synthesized. In the body after phosphorylation it is combined with a protein nucleus to form an oxidizing enzyme which is believed to be present in, and essential for the vital activities of all living cells.[2] In rats a deficiency of this substance causes retardation of growth, chronic

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[2] BOOHER, L. E.: Chemical aspects of riboflavin, Jr. Am. Med. Assoc., 1938, cx, 1105–1111.

ill health, the appearance of areas of alopecia and dermatitis about the ears, neck, chest and lower legs, and the development of cataract.[3] It was obvious that a substance of such fundamental importance must be essential in human nutrition, but symptoms distinctive of a deficiency in man hitherto have eluded observation.

Recently Sebrell and Butler [4] have described a typical symptom complex which appeared in a group of individuals who were kept on the pellagra-producing diet of Goldberger and Tanner [5] supplemented by ascorbic acid and thiamin chloride and (after symptoms of pellagra appeared) nicotinic acid. In most of these individuals after three to four months, in addition to general malaise, weakness and loss of weight, lesions resembling perlèche appeared about the angles of the mouth. The mucosa at these points looked pale, then became moist and macerated but not inflamed, and was covered with a honey-colored crust which could be removed without causing bleeding. Transverse fissures appeared exactly in the angles, occasionally extending laterally for a centimeter onto the skin. Medially they extended slightly downward but did not involve the buccal mucous membrane. The lips looked intensely red along the line of closure. These observers also noted redness and a seborrheic desquamation of the skin about the nasolabial folds, the alae of the nose and about the ears and eyes. These symptoms were not influenced by nicotinic acid, but were relieved within a few days by synthetic riboflavin.

Similar lesions, often designated "angular stomatitis," have been described by a number of writers, notably by Stannus,[6] in outbreaks of deficiency diseases in the tropics. These have been regarded usually as a manifestation of pellagra, or of a deficiency of vitamin B_2 in the old sense, but not specifically as due to lack of riboflavin. Vilter, Vilter and Spies,[7] however, independently recognized the occurrence of riboflavin deficiency as a complication in their pellagra cases, and Spies, Bean and Ashe [8] have recently discussed this feature in greater detail. They confirm Sebrell and Butler's description of the lesions, and note that the condition may occur independently of or in association with beriberi or pellagra.

These authors [9] have also found that some of the patients with pellagra who were treated merely by the administration of these synthetic vitamins

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continued to complain of nervousness, irritability, abdominal pain and marked weakness, although the specific manifestations of pellagra and beriberi were relieved. In four such cases they report that the intravenous injection of 50 milligrams of synthetic Vitamin B_6 afforded dramatic relief of these symptoms within twenty-four hours.

What other deficiencies may also lurk in the pellagra-producing diet can be determined only by future studies. There is already ample proof that the deficiency is complex. Although nicotinic acid is invaluable in the treatment of severe cases of pellagra, the simple administration of this substance will not suffice to restore normal health and nutrition. It is most important that those who treat patients with pellagra realize the frequency of these associated deficiencies and watch for them. Many patients need thiamin, and many, probably, will need riboflavin as well.

These vitamin preparations, however, must be regarded primarily as temporary aids to be used in emergencies for the relief of acute deficiency symptoms. The ultimate aim should be the institution of an adequate, well balanced diet. Only in this way can there be any assurance of maintaining normal nutrition. The measures by means of which pellagra might be controlled are now fairly well understood. This disease, however, promises to remain a serious problem in the South unless economic conditions can be so far improved that the poorer classes can and will provide themselves with an adequate diet.

P. C.

REVIEWS

Principles of Hematology. By RUSSELL L. HADEN, M.A., M.D., Chief of the Medical Division of the Cleveland Clinic, Cleveland, Ohio; formerly Professor of Experimental Medicine in the University of Kansas School of Medicine, Kansas City, Kansas. 348 pages; 14.5 × 23.5 cm. Lea and Febiger, Philadelphia. 1939. Price, $4.50.

In its scope this book follows quite closely the usual text on hematology, but it differs notably in the manner in which the subject is handled.

In planning this book the author states that he aimed primarily "to simplify the study of the disorders of the blood for the student and physician." This he has accomplished very successfully. He has made unusually free use of graphic methods to illustrate important points in the morphology and physiology of the blood cells. Ingenious diagrams and charts, many of which are taken from various journal articles of the author, make up a large proportion of the 155 text figures.

He has stressed the point that alterations in the number and morphology of the circulating blood cells are indications of disturbed physiology of the blood forming organs. These disturbances are discussed in detail, from the standpoint of etiology, recognition, and treatment.

The technic of the simpler laboratory procedures is given in detail, and their significance is discussed. The more complicated procedures which require expert knowledge, such as supravital staining and marrow puncture, are omitted.

There are numerous photomicrographs illustrating the various types of blood cells, and films from most of the more important diseases of the blood. The symptomatology of these conditions is covered largely by means of synopses and comments on 100 selected case histories, embracing the entire field of clinical hematology.

The book is more than a mere reiteration of the elementary facts and principles of hematology. Its most distinctive feature is the original and stimulating manner in which the material is presented. It is not recommended as a compendium, but it will be of great value both to teachers and students of the subject.

P. W. C.

Histological Technique for Intracranial Tumours. By DOROTHY S. RUSSELL. vi + 71 pages, with 6 plates; 22.5 × 14 cm. Oxford University Press, London. 1939. Price $2.50.

This book will be found an excellent guide for the technic of handling and staining tissue from the nervous system. The methods presented are those which the author has selected for use in her own laboratory, and confusion is eliminated by the omission of many optional methods. In larger treatises on the subject, the uninitiated often finds difficulty in selecting the method of choice from the many modifications of technic which are usually described. The methods given are those which are generally in use in most neuropathological laboratories, and have been found satisfactory both for the study of intracranial tumors and for general study of the nervous system. The book contains concise notes for the handling, fixation, and embedding of tissues. There is a full presentation of the accepted methods for staining embedded sections. Methods for handling frozen sections are given with adequate detail. The section dealing with metallic methods is brief but to the point. The author should have included Cajal's reduced silver method for staining neurofibrils in addition to that of Bielschowsky. The chapter dealing with the rapid diagnosis of biopsy material is of interest, and an outline is given for the proper choice of staining methods for

various types of tumors. The book contains a small number of photomicrographs, which are well reproduced. A larger number of such illustrations, however, would have added to the value of the book. The book can be recommended, and will be of service in any neuropathological laboratory.

J. G. A., Jr.

Practice of Medicine. By Jonathan Campbell Meakins, M.D., LL.D., Professor of Medicine and Director of the Department of Medicine, McGill University; Physician in Chief, Royal Victoria Hospital, Montreal, etc. 1365 pages, 521 illustrations, indexed; 26 × 17.5 cm. C. V. Mosby Company, St. Louis. 1938. Price, $12.50.

The second edition of this valuable textbook of medicine continues the excellencies of the first. In a work of this type, it is always possible for a reviewer to take exception to some statements or to criticize the author's judgment in regard to omissions and inclusions. It should be mentioned that the fourth lead of electrocardiograms does not conform to recently adopted standards; however, this is noted in the legends of such figures. The author still uses the old nomenclature for bundle branch block. Sulphanilamide is rather briefly discussed as a chemotherapeutic agent. It is not to be expected that any discussion of sulphapyridine should be found in the present edition. The carotid sinus syndrome seems entitled to more attention than a brief mention in the paragraphs dealing with epilepsy. The rôle of the carotid body as a chemoreceptor active in the control of blood pressure and respiration is not mentioned in the discussion of that structure. However, no useful purpose is served by such minor criticisms, and the reviewer unreservedly recommends this work to practitioners and students.

W. S. L., Jr.

The Language of the Dream. By Emil A. Gutheil, M.D. 286 pages; 24 × 16 cm. The Macmillan Co., New York. 1939. Price, $3.50.

This book is very readable, in the sense that it is short and its language is remarkably free from the "jargon" that so confuses physicians who wish to learn something about psychiatry and psychoanalysis. In addition, the material is copiously illustrated with brief, concise and understandable case reports, diagrams and reproductions of drawings by patients.

The author is a pupil of Wilhelm Stekel, who founded a school of psychoanalysis, differing in some respects from the so-called "orthodox Freudian school." Because of these differences, followers of Sigmund Freud may object to some of the theories and interpretations presented in this book.

The book consists of seven chapters and a rather thorough bibliography. The first four chapters cover the theoretical aspects, with a very adequate description of symbols and their common meanings. In these chapters case reports and examples are freely used. The fifth chapter describes the technic of dream analysis, again with many illustrative examples. The sixth chapter discusses many neurotic conditions and how they specifically influence dreams. The last chapter is devoted to a consideration of the differing schools of psychoanalytic thought with especial reference to their use and interpretation of dreams.

For physicians who wish to learn something about the psychoanalytic theories regarding the meaning and interpretation of dreams, particularly regarding their use in psychotherapy, this is about the best introductory book the reviewer has seen.

H. W. N.

Insulin: Its Chemistry and Physiology. By HANS F. JENSEN, PH.D. xii + 252 pages; 16 × 23.5 cm. The Commonwealth Fund, New York; Oxford University Press, London. 1938. Price, $2.00.

In this small monograph Dr. Jensen has successfully "endeavored to give a comprehensive review of the latest developments in the chemical and physiological investigations of insulin." The fact that over 1300 separate references have been consulted up to 1938 attests to the thoroughness of the author's work. While emphasis is placed on the chemistry and physiological action of insulin, adequate chapters are also given on the history, preparation, standardization and administration of this drug. In addition every physician will be interested in reading the chapter on insulin substitutes. Noteworthy is the warning that blood sugar reducing substances should be subjected to thorough animal experimentation before administration to the diabetic patient. Dr. Jensen's monograph can be heartily recommended to all readers interested in this fascinating subject.

E. G. S.

COLLEGE NEWS NOTES

Gifts to the College Library

The following gifts to the College Library of publications by members are gratefully acknowledged:

Books

Dr. Alpheus F. Jennings, F.A.C.P., Detroit, Mich., "Typhoid Fever" (by the late Charles G. Jennings, M.A.C.P.);
Dr. Wallace M. Yater, F.A.C.P., Washington, D. C., "Fundamentals of Internal Medicine."

Reprints

Dr. Hugo O. Altnow, F.A.C.P., Minneapolis, Minn.—11 reprints;
Lt. Col. C. L. Beaven, F.A.C.P., (MC), U. S. Army—1 reprint;
Dr. Louis F. Bishop, Jr., F.A.C.P., New York, N. Y.—2 reprints;
Dr. Joe P. Bowdoin, F.A.C.P., Atlanta, Ga.—3 bulletins, 1 mimeographed report;
Dr. Ralph Bowen, F.A.C.P., Oklahoma City, Okla.—1 reprint;
Dr. Grafton Tyler Brown, F.A.C.P., Washington, D. C.—2 reprints;
Dr. George H. Coleman, F.A.C.P., Chicago, Ill.—1 reprint;
Capt. James H. Forsee, F.A.C.P., (MC), U. S. Army—3 reprints;
Dr. Irving Greenfield (Associate), Brooklyn, N. Y.—3 reprints;
Dr. F. F. Gundrum, F.A.C.P., Sacramento, Calif.—1 reprint;
Dr. W. Hiemstra, F.A.C.P., Minneapolis, Minn.—1 reprint;
Dr. Mendel Jacobi, F.A.C.P., Brooklyn, N. Y.—16 reprints;
Dr. Jerome G. Kaufman (Associate), Newark, N. J.—1 report of a study, "New Jersey and the Cardiac Child";
Dr. E. B. Krumbhaar, F.A.C.P., Philadelphia, Pa.—Chapter 8, "Lymphatic Tissue," from "Problems of Ageing: Biological and Medical Aspects";
Dr. F. LeBlanc (Associate), Elgin, Ill.—1 reprint;
Dr. George M. Lewis, F.A.C.P., New York, N. Y.—3 reprints;
Dr. H. R. Litchfield, F. A. C. P., Brooklyn, N. Y.—3 reprints;
Dr. T. P. Lloyd, F. A. C. P., Shreveport, La.—1 reprint;
Dr. Charles E. Lyght (Associate), Northfield, Minn.—duplicate copy, "Eighth Annual Report of the Tuberculosis Committee of the American Student Health Association";
Major H. P. Marvin, F.A.C.P., (MC), U. S. Army—1 reprint;
Dr. Willard D. Mayer, F.A.C.P., Detroit, Mich.—1 reprint;
Dr. M. Hill Metz (Associate), Dallas, Tex.—2 reprints;
Dr. William Gerry Morgan, F.A.C.P., Washington, D. C.—1 reprint and a full series of "Annals of Medical History," January, 1929, to November, 1932;
Dr. William B. Rawls, F.A.C.P., New York, N. Y.—3 reprints;
Dr. Ada E. Schweitzer, F.A.C.P., Indianapolis, Ind.—1 reprint;
Dr. Donald S. Smith (Associate), Pontiac, Mich.—1 reprint;
Dr. Dudley C. Smith, F.A.C.P., Charlottesville, Va.—8 reprints;
Dr. Frederick R. Taylor, F.A.C.P., High Point, N. C.—1 reprint;
Dr. Henry H. Turner, F.A.C.P., Oklahoma City, Okla.—4 reprints;
Dr. Samuel Weiss, F.A.C.P., New York, N. Y.—3 reprints;
Dr. Hugh G. Whitehead, Jr. (Associate), Baltimore, Md.—1 reprint;
Dr. John Zarit (Associate), Denver, Colo.—1 reprint.

New Life Member

Dr. Edward L. Tuohy, F.A.C.P., Duluth, Minn., became a Life Member of the College on May 4, 1939.

Dr. Rock Sleyster, F.A.C.P., and Governor of the College for Wisconsin, was made President of the American Medical Association at its recent annual session at St. Louis.

Dr. James B. Herrick, F.A.C.P., Chicago, who served for several years on the Board of Regents of the College, was awarded the distinguished service medal of the American Medical Association at its convention in St. Louis on May 15 for his discovery of coronary thrombosis and his contributions toward the cure of heart disease.

Dr. Edward L. Bortz, F.A.C.P., and Governor of the College for Eastern Pennsylvania, during May was elected to the Presidency of the Philadelphia County Medical Society.

Dr. D. O. N. Lindberg, F.A.C.P., Medical Director and Superintendent of the Macon County Tuberculosis Sanatorium, Decatur, Ill., was elected President of the Illinois Tuberculosis Association at its annual session, Peoria, April 24–25, 1939.

Dr. G. Philip Grabfield, F.A.C.P., Boston, has been elected Secretary of the American Society for Pharmacology and Experimental Therapeutics for 1939–40.

The American Association of Clinical Pathologists, meeting in St. Louis May 13, conferred its Burdick Award, a gold medal given annually for outstanding contribution to medical science, upon Dr. Harry Goldblatt (1938 Phillips medalist of the College), Professor of Experimental Pathology of the School of Medicine and Associate Director of the Institute of Pathology, Western Reserve University, Cleveland. The honor was announced at the convention banquet of the Association, together with citation of Dr. Goldblatt's researches in hypertension and his discoveries of relationships between high blood pressure and diseases of the kidneys.

Dr. C. H. Cocke, F.A.C.P., Governor of the College for North Carolina, delivered the Lewis Burgin McBrayer address before the North Carolina State Medical Society meeting during May, his subject being "Lewis Burgin McBrayer and the State Sanatorium." This marks the founding of an annual address in honor of the late Dr. Lewis Burgin McBrayer, F.A.C.P., who for many years was the Secretary of the North Carolina State Medical Society and Managing Director of the North Carolina Tuberculosis Association.

Meeting of Maryland Chapter of the College

On May 13, 1939, Fellows and Associates of the College residing in Maryland held a sectional meeting at the Maryland Club, Baltimore, for the purpose of receiving reports from those who attended the Annual Session of the College at New Orleans. The Maryland group is organized locally with a president and secretary. Dr. Louis Krause, F.A.C.P., and Dr. W. Halsey Barker (Associate), both of Baltimore, were elected President and Secretary, respectively, for 1939–40. The Maryland members hold two sectional meetings a year, one with a scientific program and social evening

and one almost wholly of a social character, with dinner and reports on College activities.

Correction—Registration at New Orleans Session

In the statement of registration at the recent New Orleans Session of the College, published last month in these columns, the State of Mississippi was inadvertently omitted and the registration for the State of Missouri incorrectly recorded. The corrected figures follow:

	Members	*Guest Physicians*	*Exhibitors*	*Total*
Mississippi	14	2		16
Missouri	24	3	9	36

The corrected re-capitulation of the total attendance is as follows:

896	Members
525	Guest Physicians
10	Guest Non-Physicians
499	Medical Students
167	Exhibitors
578	Ladies
6	Miscellaneous
2,681	Total

MINUTES OF THE BOARD OF REGENTS

New Orleans, La., March 26, 1939

The first meeting of the Board of Regents, held in connection with the Twenty-third Annual Session of the American College of Physicians, occurred on March 26, 1939, at the Municipal Auditorium, New Orleans, La., presided over by President William J. Kerr, with Mr. E. R. Loveland acting as Secretary, and with the following present:

William J. Kerr, *President*
O. H. Perry Pepper, *President-Elect*
James B. Herrick, *First Vice-President*
Charles T. Stone, *Third Vice-President*
William D. Stroud, *Treasurer*
George Morris Piersol, *Secretary-General*
Walter L. Bierring
James D. Bruce
Egerton L. Crispin
James Alex. Miller
Francis M. Pottenger
David P. Barr
Ernest B. Bradley
Roger I. Lee
Sydney R. Miller
Robert A. Cooke
Ernest E. Irons
D. Sclater Lewis
Hugh J. Morgan
James E. Paullin
Maurice C. Pincoffs
Charles H. Cocke

Specially invited guests to this meeting included, from the Committee on Postgraduate Education, Dr. C. Sidney Burwell and Dr. Joseph A. Capps; also Dr. William D. Cutter, Secretary of the Council on Medical Education and Hospitals of the American Medical Association. The only absentees from the Board of Regents were Dr. Noble Wiley Jones and Dr. Walter W. Palmer.

The Executive Secretary read an abstract of the Minutes of the preceding meeting of the Board of Regents, which was approved as read.

Instead of following the regular order of business, President Kerr brought up immediately for discussion the subject of Postgraduate Education, and called upon Dr. Hugh J. Morgan, Chairman of the Committee on Postgraduate Education, to open the discussion, presenting his report and recommendations.

Dr. Morgan first reported upon the recent Postgraduate Courses sponsored by the College at St. Louis, Chicago and Baltimore. A total of 118 attended the Courses, coming from thirty-four different States, from Hawaii and from two Provinces of Canada. Dr. Morgan then proceeded to a report of the activities of his Committee since the last meeting of the Board of Regents. He recalled that in accordance with directions of the Board of Regents at its meeting, December, 1938, two members of the Committee on Postgraduate Education of the College went to Chicago, where they attended a meeting called by Dr. W. C. Rappleye, on the authorization of the Association of American Medical Colleges, to consider the advisability of the formation

of a National Council on Medical Education, Licensure and Hospitals. Dr. Morgan's further report herewith follows:

REPORT, COMMITTEE ON POSTGRADUATE EDUCATION

"A meeting was called by Dr. W. C. Rappleye on the authorization of the Association of American Medical Colleges to consider the advisability of forming a National Council on Medical Education, Licensure and Hospitals. The representatives convened in Chicago February 11, 1939. Hugh J. Morgan and Edson W. Carr (alternate; Chicago) represented the College of Physicians.

"The representatives of the several organizations assembled in Chicago February 11, prior to the annual Congress on Medical Education and Licensure. All of the organizations which had been invited to send representatives did so with the exception of the A. M. A. A letter from Secretary Booth of the Board of Trustees of the A. M. A. was read by Dr. Rappleye, stating that the formal invitation of the Association of American Medical Schools to the Trustees of the A. M. A. was, unfortunately, not delivered to the Trustees. Therefore, the Trustees of the A. M. A. had received no invitation and had appointed no representatives. Dr. Booth stated that the Council on Medical Education and Hospitals had considered the matter and would doubtless be represented. Dr. Wilbur, Chairman of the Council, appeared in the meeting at this point and announced that he represented neither the Council on Medical Education and Hospitals nor the Board of Trustees of the A. M. A. and asked if he might attend as an "unofficial observer." He was welcomed warmly by acting chairman Rappleye.

"The advisability of forming a new organization with wide representation was discussed. It was generally agreed that this was desirable and a resolution was adopted to the effect. The purpose of the organization was defined, by resolution, as follows:

"'The Council is created to meet the need of a body representing the medical profession, the universities, medical schools, hospitals, licensing bodies, specialty boards, public health agencies, and other national organizations in this country which deal with different phases of medical education. The Council shall serve as a clearing house for the coöperative consideration of those problems and programs of professional training with which more than one organization is concerned; as a medium for consultation and mutual assistance in the formulation and support of adequate educational standards; and as an agency for advice and recommendations to member and other organizations dealing with medical education.'

"Many representatives, including those of the College of Physicians, felt that, if this body was to act "as a clearing house for the coöperative consideration" of problems, it was essential that the A. M. A. be represented and take part in the organization of the body (the selection of its name, the writing of its constitution, etc.). Further action was delayed therefore to attend upon the action of the A. M. A. A committee was appointed to confer with the Council on Medical Education and Hospitals to inform them that:

"(1) It is the opinion of the representatives that an advisory board is desirable, to function in the field defined by the resolution;

"(2) The representatives feel it a matter of great importance that the A. M. A., which has through its Council accomplished so much in the field, participate in the organization and administration of such an advisory body.

"The meeting adjourned with the request from the acting chairman that the representatives inform their respective organizations of the action taken and invite endorsement of and participation in the proposed body.

"REPRESENTATIVES APPOINTED TO ATTEND MEETING ON FEBRUARY 11, 1939, TO DISCUSS THE PROPOSED NATIONAL COUNCIL ON MEDICAL EDUCATION, LICENSURE, AND HOSPITALS

Association of American Medical Colleges

William S. Middleton, Madison
Willard C. Rappleye, New York
Maurice H. Rees, Denver

American Hospital Association

Robin C. Buerki, Chicago
M. F. Griffin, Cleveland
Christopher Parnall, Rochester, N. Y.

The Catholic Hospital Association

Federation of State Medical Boards of the U. S. A.

Walter L. Bierring, Des Moines
J. W. Bowers, Fort Wayne
Harold Rypins, Albany

Advisory Board for Medical Specialties

Franklin G. Ebaugh, Denver
John Green, St. Louis
B. R. Kirklin, Rochester, Minn.

National Board of Medical Examiners

Waller S. Leathers, Nashville

American College of Surgeons

Arthur W. Allen, Boston
Dallas B. Phemister, Chicago

American College of Physicians

Edson W. Carr, Chicago
Hugh J. Morgan, Nashville

Association of American Universities

E. B. Fred, Madison
C. S. Yoakum, Ann Arbor

American Public Health Association

Waller S. Leathers, Nashville

American Association for the Advancement of Science, Division of Medical Sciences

Anton J. Carlson, Chicago (absent)"

Summarizing his report, Dr. Morgan made the following recommendations:

(1) That the College of Physicians approve the purpose of an Advisory Council of Education, Licensure and Hospitals, adopted by several organizations, whose representatives met in Chicago on February 11, 1939;

(2) That two representatives of the College be appointed to attend and participate in the organization meeting and subsequent deliberations of the Advisory Council;
(3) That our representatives in this Advisory Council state our interest in the subject of graduate training in internal medicine and allied specialties, asking the Council for suggestions as how best to proceed.

President Kerr explained that no positive action on the recommendations was to be taken at this meeting of the Board, but the matter was presented for due consideration and thought from every standpoint. He introduced Dr. William D. Cutter, Secretary of the Council on Medical Education and Hospitals of the American Medical Association, who addressed the Board as follows:

"Mr. President, and members of the Board of Regents, I would like to confirm what Dr. Morgan has already told you about the desire, on the part of the Council on Medical Education, to collaborate with the American College of Physicians and with the American Board of Internal Medicine, insofar as this problem of graduate education in the field of Internal Medicine is concerned. We have seen a very successful illustration of such collaboration carried out in the American Board itself, which is jointly the responsibility of the College and the Section on Medicine of the American Medical Association, and we feel there is every reason to believe, in the light of our experience of the last few years, that such coöperation between the Council and various specialties will prove to be, in the long run, the satisfactory way to deal with problems. It is a fact that a number of the specialty boards, representing specialties, have already tried independently to formulate standards and give approval to different courses in institutions, residencies, etc., in the specialty fields. With some experience of their own, these men are turning to the Council and asking for assistance. We have entered into definite plans of coöperation with the Board of Radiology and Pathology. The people in the field of Ophthalmology and Otolaryngology have expressed a desire to confer with us in regard to plans.

"Perhaps I could make more plain to you what we are talking about if I describe somewhat in detail the plan of collaboration which we have with the Board of Pathology and Radiology. There should be definite means of determining standards of education, training, apprenticeship and other courses which will enter into the training for specializing in these fields. These standards should be formulated by means of conference between representatives of our Council and representatives of specialty societies. The standards and requirements, minimum requirements, were determined and the types of courses to be approved were agreed upon and the Council and specialty group conferred. Collection of information and investigation of hospitals would be better conducted by the Council and its staff, but the plan mentioned is the plan that seemed agreeable to them. After the information was collected, after the institutions were visited and reports made, covering all the points agreed upon as important and essential, we again went into conference with the representatives of the specialty group to determine how that evidence should be evaluated; how courses are to be approved, which approved and which not approved, and then after we reach an agreement in regard to these facts, they are free to publish in any way they see fit, the result of deliberation and equally we will use the channels of publicity of the American Medical Association to make known these institutions and courses acceptable to the specialty groups.

"The reason, I think, why these boards have come to us seeking this form of collaboration is that, in their own experience, they have encountered difficulties. When it is up to a specialty board, for instance, dermatology, to make approval for facilities of graduate training in its field, they do not have a permanent or trained staff of inspection. They depend upon their one board and the members cannot give the proper time to it. A member is asked to visit a few schools in the neighborhood

where he resides and others are asked to make inspection in other regions. There is no uniform inspection or standard. Formulation of opinions are many times influenced by personal factors. For instance, the Board of Otolaryngology and Ophthalmology published a list of residencies recently which they approved. We have published the list we approved. In most part, these lists coincide. There were a few discrepancies which we examined with care to find reasons for discrepancies. I think I can tell you that we have found in every case where these specialty boards have approved institutions which we did not approve, it was because of personal relationship or due to the fact that sufficient time was not taken to go deeply into the situation. On the other hand, where some were approved by us and not by them, we found that this also was due to lack of personal acquaintance with the man at the head of the institution or failure to go deeply into the character of the service. We came to the conclusion, as well as they, that the actual business of making inspection and collecting evidence is better carried out by our staff.

"Another thing, if each one of the specialty boards took up the work of conducting their own investigation there would be a multiplicity of inspection, to which the institutions would rebel. Some of them have expressed dissatisfaction with this condition in which so many different agencies attempt to make investigations, for approval of hospital services and courses of training. So it seems to us that the actual business of collecting information could be better carried out through a single agency, which is already in existence and is familiar with the work. After the information is collected, the Council again confers with the specialty concerned with respect to the evaluation of the evidence. When we have gotten evidence with regard to a service, for instance, dermatology, we sit down with representatives of the board and go over the evidence with them and determine together just exactly which institutions should be approved and which should not be approved. After an agreement is reached about that, we can publish a list with the satisfaction of knowing that the residencies and other courses approved will be acceptable to the specialty societies and specialty boards interested in that field.

"That is the proposal we would like to make to the American College of Physicians. Your Committee, or certain members of the Committee, could consider with us what the essential factors are that go to make up a worth while residency and graduate course in the field of internal medicine. It is not difficult to write an agreement about that. All of the work will go for the same thing, and it will be inevitable that we can arrive at a satisfactory agreement as to what the important elements should be in rating apprenticeships. The kind of training and matters of personnel should be included in the study. Investigation of these institutions, if it meets your approval, can be made when making other investigations. When inspecting a hospital, we can cover all the specialties at one time and submit a report to you concerning evidence which we secure and we can decide what is to be done about it. This sort of collaboration would simplify the work of both organizations. We would not undertake to pass judgment on all the details of specialty training; on the other hand, the public will have greater confidence in this kind of work if not conducted by specialty groups, that might be interested in furthering their own importance and welfare.

"If it is possible for us to join with the College of Physicians in a program of this sort, leading to comprehensive study for graduate study, and proper appraisal of same, in which you yourself will have a part, we shall be very happy indeed to join with you in this kind of enterprise. We hope that we may have the opportunity to discuss this further at a meeting in Chicago, which has been proposed."

In questions and answers following Dr. Cutter's remarks, it was revealed that there is no relationship or plan of coöperation between the work of the Council on Medical Education and Hospitals and the American College of Surgeons. The college of Surgeons has initiated its own independent program of appraisal of educational facilities. It was also revealed that the Council on Medical Education and Hospitals

is composed of seven members, each appointed for a seven-year term. Appointments are made by the President of the American Medical Association. The Council is responsible to the House of Delegates. The Council on Medical Education and Hospitals did not participate in the meeting called by Dr. W. C. Rappleye at Chicago, February 11, 1939, concerning the formation of a National Council on Medical Education, Licensure and Hospitals, only because it had no authority from the House of Delegates of the American Medical Association. It was anticipated that the House of Delegates will issue instructions after its meeting in May of the current year.

Dr. Joseph A. Capps, the other representative of the College at the Rappleye meeting in Chicago, expressed the sentiment that our College should move slowly in the matter and consider many propositions before adopting final action. He pointed out that the new Council is an advisory one and not an executive body, and that our problem is to settle on some agency that can carry to execution the things we require. Dr. Capps said it was self-evident that this should be done by one body, and that if that might be the Council on Medical Education, he thought it would be desirable. Dr. Capps pointed out that two members of the American College of Physicians are already on the Council, and that whereas the present Council members are appointed by the President of the American Medical Association, it would be advantageous to have the By-Laws amended to permit the Council on Medical Education and Hospitals to make nominations, which would later be approved by the House of Delegates.

Dr. Roger I. Lee explained that the Council on Chemistry and Pharmacy of the American Medical Association is a Council of the Board of Trustees of that body, and its members are appointed by the Trustees. The Council on Medical Education and Hospitals is a Council of the House of Delegates. Dr. Lee further deplored the duplication of activity on the part of so many agencies engaging in the same work, pointing out that the American Medical Association conducts a very elaborate survey of hospitals, including the certification of hospitals for internship.

Dr. Ernest E. Irons recommended that the American College of Physicians move slowly and review the possibilities for working with the Council on Medical Education and Hospitals.

Dr. C. Sidney Burwell made two points: first, agreeing that a single body should rate hospitals, and, second, that the problem of graduate education, the problem of training men for the practice of specialties, is an enormously complex one, and that various bodies have gone ahead without sufficient consideration of the ultimate ends. He agreed that the American College of Physicians has a large and proper interest in the matter, and that medical schools have a secondary interest and that the hospitals also have a great interest, because they will be called upon to play a large part. Likewise, licensing boards and public health organizations will be concerned with the problem. Dr. Burwell asked for coördination of all of these interests, and recommended adequate time before reaching a decision on the manner in which the College would participate.

At the request of Dr. Roger I. Lee, Dr. William D. Cutter reported that the Council on Medical Education and Hospitals is made up of the following members:

Dr. Ray Lyman Wilbur, Chairman, San Francisco
Dr. John H. Musser, New Orleans
Dr. Fred Moores, Des Moines
Dr. Reginald Fitz, Boston
Dr. Fred W. Rankin, Lexington
Dr. Charles Gordon Heyd, New York
Dr. F. H. Lahey, Boston
Dr. William D. Cutter, Chicago

Dr. Cutter explained that the American Medical Association has no other agencies than the Council on Medical Education which are directly concerned with medical

education or the supervision of hospitals. The Association has never assumed responsibility for licensure, because this has been considered a State function and governed by the laws of the several States. The Council on Medical Education, Licensure and Hospitals, proposed by Dr. Rappleye, is to be purely an advisory one, not executive or administrative. It is proposed to be a clearing house for information, for conferences and discussion. It would have no power to control or direct any agencies which have representation in the Council on Medical Education and Hospitals. The field proposed goes no further than the Council on Medical Education and Hospitals, except in the matter of licensure. The Council on Medical Education does not make inspection of medical schools or hospitals except upon invitation.

Dr. Maurice C. Pincoffs inquired if the Council on Medical Education and Hospitals intends to add to its personnel men qualified for making the type of hospital and graduate education survey our College is interested in, or whether the Council is of the opinion that a group of experienced surveyors can survey any field.

Dr. Cutter replied that the Council's investigators would be instructed by special representatives, who would first be informed through advice from the specialty groups. Should this be inadequate, the Council would do the job over again to the satisfaction of the groups interested. Already some of the specialty boards have been invited to send representatives on some of the inspection tours, in order that they may see how the inspections are done and in order that they may instruct the Council how to improve its work. Dr. Cutter explained that no new machinery has yet been set up, but that informal conferences with representatives of interested boards will be arranged. Dr. Cutter also explained that while hospitals are not specifically graded, there are three types of recognition: first, approval for the training of interns; second, approval for training residents for advanced types of education (there are so many specialty fields that some hospitals have many different residencies; a hospital may be approved for some and not other types of residencies); third, admission to the register. This latter includes six thousand hospitals. The admission to the register is done on the basis of correspondence, official reports and investigations by doctors in the locality. The Council has three men who devote themselves exclusively to hospitals; one additional man who devotes his time chiefly to hospitals; and one additional man who devotes his time chiefly to graduate medical education outside of hospitals.

President Kerr discussed the invitation from the Trustees of the American Medical Association for a joint meeting with the Regents of the American College of Physicians, and suggested the possibility of such a meeting being held, at the convenience of the Trustees of the American Medical Association, at Chicago on April 29.

Dr. Hugh J. Morgan, Chairman of the Committee on Postgraduate Education of the College, inquired if our College should merge its interest in support of the Council on Medical Education and Hospitals; insofar as work is concerned in graduate training and medical specialties, could the College do that in a conspicuous fashion? Would it be difficult for the College to do more than simply support and advise with the Council, and would the project in the final analysis be a Council job in the future as in the past? Does the Council on Medical Education and Hospitals feel that specialty training is in its province? Is the American Medical Association, with so many doctors, really concerned with specialty training? Has the American Medical Association been particularly interested in the development of specialties? Have the specialty sections in the American Medical Association been a natural, spontaneous development? Should not specialty training be the natural concern of specialty societies and hospitals, or is it proper that a body dominated by general practitioners should be concerned with specialty training? Would it be reasonable for the College to postpone its decision as to how to proceed in the field of graduate training until after the Advisory Council on Medical Education, Licensure and Hospitals is or-

ganized? Would it be consistent for the College to go into the Advisory Council on one hand and make a decision without consulting the Advisory Council on the other, when the Advisory Council is being formed to act as a clearing house of problems of professional training?

DR. WILLIAM D. CUTTER: "I will be glad to answer these questions. I think we can get further in this intimate discussion.

"I am tremendously interested in this problem and am gratified by the response this afternoon.

"The first question Dr. Morgan asked was whether the part which the College of Physicians would play would be recognized. I think I can say without hesitation that the Council and the American Medical Association would give the fullest publicity to the fact that the College of Physicians had collaborated in this effort. I do not know whether that kind of publicity would be sufficient to be satisfactory from your point of view, but I am certain that by every avenue of publicity we will be glad to call attention to the fact that this is a joint enterprise in which the College has contributed.

"The second question as to whether the American Medical Association, which is an organization of so many doctors, is an organization which, by its very nature can be interested in the problems of the specialties. My answer is unequivocally and emphatically, yes. Medicine is medicine and no part of medicine can exist apart from medicine, and we believe as firmly as we can believe anything, that the American Medical Association is not only interested, but is responsible for every phase of medical activity, including all specialties and insofar as the sections are concerned, they have not been created by means of any force or pressure from the outside. The difficulty we have had is to keep down the number of sections. Many groups demand recognition. Sometimes this recognition has been given and after a few years the meeting dwindled. No effort on the part of the American Medical Association, as a whole, has been made to stimulate the creation of new sections. What we have is the response from the men in special fields."

President Kerr thanked Dr. Cutter for his attending the Regents' meeting and for the information he had furnished, at which time Dr. Cutter retired and the meeting proceeded with the regular order of business.

The Executive Secretary presented the following communications: (1) Dr. Cecil Striker, Cincinnati, Ohio, pointing out a disproportionate ratio of invited guests as against members appearing on the New Orleans program; (2) Dr. Julien E. Benjamin, Cincinnati, Ohio, concerning guest speakers, repetition of speakers on the program of clinics and demonstrations at the New Orleans Session.

Dr. James B. Herrick presented a communication from Dr. Noble Wiley Jones, of Portland, Ore., who was named official representative of this College to attend the inauguration of the Australasian College of Physicians at Sydney, during December, 1938. Dr. Herrick reported that Dr. Jones had attended that meeting, delivered an address and took part in the activities, and received an honorary degree. Dr. Jones had submitted a full report to President Kerr, who, in turn, had submitted it to Dr. Herrick for comment and review. Dr. Jones' five concrete suggestions were read by Dr. Herrick, after explaining that the background for the suggestions was furnished by Dr. Jones being impressed by the importance of keeping in close touch with the English speaking physicians of the world, and feeling that this can be done in several ways. His suggestions follow, with Dr. Herrick's comments indicated in parentheses at the end of each suggestion:

(1) That the American College of Physicians exercise its influence—which would be indirect—to secure Exchange Professorships in medicine and pathology between the Australasian and American Medical Schools. He states that he has met men in Australia whose presence would bring honor to any American school they visited. (I see no objection to this.)

(2) That each year an invitation be extended to an Australasian medical man to take part in our annual session as a guest speaker of the College. As these men are usually full-time workers, on salary, it would be necessary for the American College of Physicians to assume at least part of their expenses. (I think this is all right if he will say " from time to time " instead of each year.)

(3) That the Executive Secretary communicate with the Hon. Secretary of the Royal Australasian College of Physicians each year, six months before the annual meeting of the American College of Physicians, informing him of the date and place of our meeting and invite its members to attend. (Surely no objection to that.)

(4) That an effort on the part of our members be made to attend the annual meetings of the Royal Australasian College of Physicians. They will be repaid many-fold in pleasure, information and a mutual understanding with the Australasian people. (There is no objection to this, I am sure.)

(5) That The American College of Physicians establish an annual prize of a small sum of money, that is, $100.00, or better $400.00, to be controlled by the Royal Australasian College of Physicians, and to be presented to a new or recent graduate of any of the medical schools in Australia presenting the best thesis based on original work in medicine or pathology.

Dr. Herrick was not in favor of the last suggestion, because he felt it an artificial way of stimulating men to work, and that it would establish a bad precedent to offer this money as a reward to some young man who presented a thesis, the merits of which would be decided upon by the Australians themselves. He therefore recommended that this suggestion be entirely omitted.

Dr. Herrick went on to state that Dr. Jones had expressed the hope that our College will do everything possible toward entertaining and assisting members of the Royal Australasian College of Physicians when they come to this country. Dr. Herrick expressed the opinion that the Executive Secretary, through the College office, could perform these courtesies, as he has already done in arranging a program and furnishing introductions for one of the Fellows of the Royal Australasian College who is visiting this country this May. Dr. Herrick said that Dr. Jones' report indicated that his mission to Australia had as one of its objectives the establishment of a feeling of goodwill and mutual understanding between members of the two Colleges directly and between the peoples of the two countries indirectly. Dr. Jones had been convinced over many years that it would be important for all English speaking nations to stand together for the preservation of their form of government, their culture and their civilization, and that the people of Australia have the same outlook. Dr. Herrick reported that he had already written to Dr. Jones, expressing the thought that the Regents must be careful in pledging the College in non-professional matters, and that the College ought not to take action along this line. Dr. Herrick recommended that the College thank Dr. Jones for his suggestions and recommendations concerning his visit to the inauguration of the Royal Australasian College of Physicians, and that our Committee on Fellowships and Awards consider the recommendation of offering a prize to any one in the world.

On motion by Dr. Herrick, seconded by Dr. Roger I. Lee, and unanimously carried, it was

RESOLVED, that the recommendations presented by Dr. Herrick be approved.

President Kerr then presented a communication in the form of a telegram and letter from Dr. Olin West of Chicago, inviting the Regents of the American College of Physicians to meet with the Board of Trustees of the American Medical Association for the purpose of discussing a program of graduate education. It was pointed out that the College would be interested only in this particular matter and not in medical economics. The invitation, however, included hospital service, group hos-

pitalization plans, some phases of the problem of economics; the invitation being meant primarily for a joint meeting to talk over common problems between the two organizations. After general discussion, decision on the acceptance of the invitation and the date of the meeting was postponed, until the succeeding meeting of the Board of Regents.

Dr. Sydney R. Miller, Chairman of the Committee on Credentials, presented the report of that Committee in two parts: (1) he distributed a mimeographed list of the candidates for Fellowship and Associateship as recommended for election by the Committee on Credentials on February 26, 1939. There were 43 advancements from Associateship to Fellowship, 10 to be elected directly to Fellowship, 8 deferred for further information and 1 rejected, making a total of 62 candidates for Fellowship that had been acted upon. There were 61 candidates recommended for election to Associateship, 8 deferred and 13 not qualified, making a total of 82 candidates for Associateship that had been acted upon; (2) Dr. Miller then distributed the list of candidates reviewed on the morning of March 26, consisting of (a) 64 candidates for Fellowship, of which 18 were recommended for direct election, 37 were recommended for advancement, 5 were deferred for further credentials and 4 were rejected; (b) 83 candidates for Associateship, of which 2 were recommended for election directly to Fellowship, 70 were recommended for election to Associateship, 6 were deferred and 5 rejected.

Dr. Miller answered questions from the Board of Regents concerning any candidates and explained, where inquiries arose, why candidates were not recommended for election.

On motion by Dr. Sydney R. Miller, seconded by Dr. George Morris Piersol, and regularly carried, it was

RESOLVED, that the following list of 110 candidates be and herewith are elected to Fellowship in the American College of Physicians: (This list was published in the April, 1939, issue of this journal).

On motion by Dr. Sydney R. Miller, seconded by Dr. William D. Stroud, and regularly carried, it was

RESOLVED, that the following list of 131 candidates shall be and are herewith elected to Associateship in the American College of Physicians: (This list was published in the April, 1939, issue of this journal).

On motion by Dr. O. H. Perry Pepper, seconded by Dr. F. M. Pottenger, it was

RESOLVED, that the Chairman of the Committee on Credentials and the Executive Secretary proceed with the revision of the informative booklet concerning criteria for membership and the revision of the proposal form.

In the discussion that followed, Dr. Sydney R. Miller explained that this had been authorized by the Regents at the preceding meeting, but that there had not been adequate time or opportunity to complete the work. The booklet has become obsolete, and it lacks clarity, and it is proposed to thoroughly revise it and improve its appearance.

Dr. James E. Paullin, Chairman of the Committee on Public Relations, presented complaints against a Fellow of the College whose writings in a semi-popular journal were considered derogatory and not in keeping with the dignity and purposes of the American College of Physicians.

The Committee on Public Relations was instructed by the Board of Regents to bring the matter to the attention of this member in an effort to have him desist from this activity, or to present his resignation.

Dr. George Morris Piersol, Secretary-General, reported the following deaths since the last meeting of the Board of Regents, making a total since the last Annual Session of the College of twenty-nine Fellows and four Associates:

Fellows:

Berg, Henry W., New York, N. Y., December 22, 1938
Boettiger, Carl, Flushing, L. I., N. Y., February 1, 1939
Gregg, Donald, Wellesley, Mass., January 6, 1939
Kauffman, Lesser, Buffalo, N. Y., March 11, 1939
Parramore, James Otho, Crown Point, Ind., January 24, 1939
Stark, Morris, New York, N. Y., July 18, 1935

Associates:

Esler, James W., Washington, D. C., December 15, 1938
Kalteyer, Fred J., Philadelphia, Pa., December 21, 1938

Dr. Piersol then reported the following additional Life Members since the last Regents' meeting in December, 1938:

O. H. Perry Pepper, Philadelphia, Pa.
Charles Hartwell Cocke, Asheville, N. C.
Andrew H. Hangarter, Brooklyn, N. Y.
Richard Arminius Kern, Philadelphia, Pa.
Edward Bridge Bigelow, Worcester, Mass.
James B. Herrick, Chicago, Ill.
William S. Baldwin, Lorain, Ohio
Lawrence Getz, Ancon, Canal Zone
Clifford P. Rutledge, Shreveport, La.
Mortimer Warren, Portland, Maine
Frank Bethel Cross, Brooklyn, N. Y.
James Alexander Lyon, Washington, D. C.

At the meeting of the Board of Regents on December 18, 1938, he had reported four Life Members, which makes a total for the year, since the last Annual Session, of 16, or a grand total of 117, of whom 8 have died, leaving a balance of 109 living Life Members.

On motion seconded and unanimously carried, the report of the Secretary-General was accepted.

Dr. Maurice C. Pincoffs made a brief report as the Editor of the ANNALS OF INTERNAL MEDICINE. Due to an increase allowed in his budget, he had been able to add to the office personnel and greatly facilitate the handling of the editorial work of the ANNALS for the future. The circulation of the ANNALS had grown approximately three hundred since the preceding Annual Session, and there has been an ever increasing number of manuscripts presented for publication.

On motion seconded and regularly carried, the report of the Editor was accepted.

Dr. Roger I. Lee, Chairman of the Committee on Future Policy, said that there was no report to be made.

Dr. William D. Stroud, Treasurer, presented the following report:

"As of March 19, 1939, our invested principal in the Endowment Fund was $68,494.98 in Bonds; our General Fund, $34,855.50 in Bonds and $57,390.95 in Stocks, making a total value of $160,751.43. The book value of that date was $161,085.00, or a profit on investments of $333.57. The income on our invested principal is averaging 4 per cent.

"During the past year there has been an increase in the total amount of our Endowment Fund plus our General Fund from $205,383.47 to $222,014.12, or a profit

of $16,630.65 for the year. Our College, therefore, has a cash plus investment value of $222,000.00, plus the value of our property in Philadelphia."

On motion seconded and regularly carried, the report of the Treasurer was accepted.

Dr. David P. Barr, Chairman of the Committee on Fellowships and Awards, had no report to present.

Dr. James Alex. Miller, Chairman of the Committee on Finance, reported as follows:

"I have here in the report of the Finance Committee, Mr. President, a detailed account of the investments. I do not think the Regents care for me to read this; however, I will do so if requested. The Finance Committee would like to emphasize again the very excellent financial situation of the College, and particularly in these troublous times that our invested funds have a market value which is definitely more than the cost value. I thought also it would be worth while to read how these are diversified: 65 per cent in bonds; 28 per cent preferred stock; 7 per cent common stock. As to the character of the various investments; public utilities 32 per cent; industrials, both preferred and common, 25 per cent; U. S. Government 17 per cent; railroad 15 per cent; foreign bonds 8 per cent; financial stock 2 per cent; municipal bonds 1 per cent.

"Since the last report to the Board of Regents, the Finance Committee has authorized the purchase of 5,000 Florida Power Corporation, First Mortgage, Series 'C,' 4s, due 1966, at a price of $4,485.90, for the General Fund; also for the General Fund, 4,000 North American Company, debentures, 3½s, 1949, at a cost of $4,175.00. For the Endowment Fund, 1,000 North American Company, debentures, 3½s, at a cost of $1,043.75; also for the Endowment Fund, 1,000 Ohio Public Service, First Mortgage, 4s, 1962, at a cost of $1,070.00 and 2,000 U. S. Treasury, 2s, 1947, at a cost of $2,045.75.

"At this present meeting the Finance Committee, as has already been reported by the Treasurer, would report that the Endowment Fund Cost Value is $68,494.98 and the General Fund Cost Value is $92,246.45, making a total of invested funds of $160,741.43. The present market value of these securities, as of March 19, was $161,085.00, showing a total investment profit, as of that date, of $333.57. These investments are diversified as follows: Bonds, 65 per cent; preferred stock, 28 per cent, common stocks, 7 per cent. As to the character of the various investments, public utilities, 32 per cent; industrials, both preferred and common, 25 per cent; U. S. Government, 17 per cent; railroad, 15 per cent; foreign bonds, 8 per cent; financial stock, 2 per cent; municipal bonds, 1 per cent.

"At this present meeting, the Finance Committee has authorized the transfer from the General Fund to the Endowment Fund of 3,000 Great Northern, 4s, Series 'H,' convertible, due July 1, 1946, this giving a total of $5,000.00 of this security in the Endowment Fund. It was voted to sell 5,000 of these Great Northern Bonds, and to buy in their place for the Endowment Fund, 5,000 Great Northern General B, 5½s, due January 1, 1952. This still leaves an uninvested sum in the Endowment Fund of a little less than $2,000.00.

"For the General Fund there being $10,000.00 available for investment, it was voted on the recommendation of the Girard Trust Company to buy 40 Shares of the Monsanto Chemical Company, 4½s, cumulative preferred, at an estimated cost of $4,-680.00, and also to buy 40 Shares of the Great Atlantic and Pacific Tea Company, 7 per cent, cumulative preferred, at an approximate cost of $5,000.00.

"The Finance Committee also voted to recommend to the Board of Regents the adoption of the following resolution:

"RESOLVED, that inasmuch as the Finance Committee reports a most satisfactory

condition of our finances and that this is due very largely to the splendid coöperation and sound recommendations made to it by the Girard Trust Company, through its Trust Investment Department, that the Board of Regents of the American College of Physicians desires to express its deep appreciation of the very efficient service that has been rendered to the College by the Girard Trust Company.

"Finally, the Finance Committee wishes to suggest to the Board of Regents that inasmuch as it has come to the knowledge of this Committee that the present policy concerning commercial exhibits might be modified to the advantage of the College, the Finance Committee would recommend to the Board of Regents that in some suitable manner, possibly through the appointment of a special committee, a thorough study be made in regard to the commercial exhibits, not only from the financial point of view, but also from that of the general interests of the College.

Respectfully submitted,

ROGER I. LEE,
CHARLES T. STONE,
WILLIAM D. STROUD,
JAMES ALEX. MILLER, *Chairman,*
Committee on Finance"

On motion seconded and regularly carried, it was

RESOLVED, that the report of the Finance Committee be accepted; that the recommendation concerning the resolution of thanks to the Investment Counsel, Girard Trust Company, be approved; that the recommendation of the appointment of a special committee to investigate commercial exhibits be referred to the present Committee on Exhibits and Advertising.

The Executive Secretary distributed to all members of the Board of Regents the Auditor's report and detailed financial statements for the year 1938, which herewith follow.

Adjournment:

Attest: E. R. LOVELAND,
Executive Secretary

MINUTES OF THE BOARD OF REGENTS

New Orleans, La., March 28, 1939

The second meeting of the Board of Regents, held in connection with the Twenty-third Annual Session of the College, was called to order on March 28, 1939, at the Municipal Auditorium, New Orleans, La., with the President, Dr. William J. Kerr, presiding, Mr. E. R. Loveland acting as secretary and with the following present:

William J. Kerr, *President*
O. H. Perry Pepper, *President-Elect*
James B. Herrick, *First Vice-President*
Charles T. Stone, *Third Vice-President*
William D. Stroud, *Treasurer*
George Morris Piersol, *Secretary-General*
Walter L. Bierring
James D. Bruce
Egerton L. Crispin
James Alex. Miller
Francis M. Pottenger
David P. Barr
Ernest B. Bradley

Roger I. Lee
Sydney R. Miller
Robert A. Cooke
Ernest E. Irons
D. Sclater Lewis
Hugh J. Morgan
James E. Paullin
Maurice C. Pincoffs
Charles H. Cocke

Abstracted Minutes of the preceding meeting of the Board of Regents were read and approved.

Dr. James E. Paullin, Chairman of the Committee on Public Relations, presented and recommended the acceptance of the resignations of Dr. William Riley Brooksher (Fellow), Fort Smith, Ark., and Major Alfred Mordecai (Associate), (MC), U. S. Army.

On motion by Dr. Paullin, seconded by Dr. Stroud, it was

RESOLVED, that the resignations of Dr. William Riley Brooksher (Fellow) and Major Alfred Mordecai (Associate) be accepted.

Dr. Paullin then reviewed four cases affecting fees and dues. A resolution was adopted providing for the waiver of dues until recovery and resumption of practice in the case of those men who were out of practice because of illness, in accordance with provisions of the By-Laws.

Dr. Sydney R. Miller, Chairman of the Committee on Credentials, continued his earlier report, reading Article IV, paragraph 2, of the Constitution, calling particular attention to the phrase, "and such additional rules as the Board of Regents may from time to time adopt": "(a) Fellows. Fellows shall be members of the medical profession engaged as practitioners, teachers or research workers in Internal Medicine, or in an allied specialty, who shall have been elected in accordance with the By-Laws and such additional rules as the Board of Regents may from time to time adopt—the By-Laws and such additional rules being intended to insure the election only of internists of such high qualifications, personal and professional, as would entitle them to be rated as fully qualified Fellows. Fellows shall be authorized to use the letters F.A.C.P. after their names on professional cards, in professional directories and in professional publications. Fellows shall have the right to vote and to hold office." Under the authority given the Regents by this section, the Credentials Committee recommended the following new rule for the advancement of Associates to Fellows: "No Associate hereinafter elected shall be eligible for consideration for Fellowship unless he or she shall have been certified by one of the American Boards for the certification of specialties." Dr. Miller pointed out that most of the specialties have certifying boards, such as those in Radiology, Pediatrics, etc. Dr. Miller pointed out that this proposal is not presented as an amendment, but that the Constitution already makes provision for additional rules and regulations adopted by the Regents.

Dr. Roger I. Lee inquired whether it might not be advisable to modify such a rule so that it would not be absolute, pointing out that there might be exceptions, that some men might not want to spend the time or money to be certified as an internist, since certification might not be of material advantage to some.

President Kerr pointed out that this new rule would not in any way alter the provision already in the Constitution and By-Laws for the admission of men directly to Fellowship who present adequate and exceptional qualifications. The proposed rule would apply only to Associates elected hereafter, and would provide a definite standard of accomplishment, professionally, during the five-year Associate term, but that mere certification in itself might not guarantee advancement to Fellowship, because the College has other requirements.

Dr. James Alex. Miller expressed sympathy with the project in mind, but indicated a hesitancy in voting for it at present. He said in part: "It is fundamentally not exactly the kind of rule that was in mind when this opportunity was offered to give the Regents extra powers. It is a fundamental change. In the next place, I wonder if we are ready to make this radical step at the present time. Thirdly, I would like to suggest that this has definite relation to our financial structure. That ought to be considered, too. I think it is a valuable thing to be brought up, and I think we ought to think it over carefully. Perhaps, it is better not to take immediate action on it, but have it brought up later as an amendment to the By-Laws, to come before the College as a body. I am in sympathy with the plan."

Dr. George Morris Piersol: "This proposal does not involve the status of present Associates. Only those elected in the future would be subject to this rule. Our present standards are not sufficiently definite. The Credentials Committee after years of struggle has been searching to find some adequate and proper yardstick to evaluate the professional standards of Fellowship. The ones at present are certainly inadequate. They have little virtue. They are absolutely not adequate criteria. This College was instrumental in setting up the American Board of Internal Medicine. The fundamental plan of certification is sound, and we were instrumental in initiating this policy, and now have a controlling hand in this Board. It seems ridiculous, after having created this and having it in operation, for us to circumvent its requirements and follow inferior standards ourselves. The Committee feels that until such a plan as this proposal is adopted, we shall never arrive at an adequate basis for determining professional qualifications. After considerable thought and deliberation, this recommendation was submitted. It does not affect the present method of electing Associates. It does make it obvious that there shall be certain things Associates shall have to do before being considered for Fellowship. It does not imply that if the Associate passes the certifying board he will be elected a Fellow, for there are other qualifications, if the By-Laws still remain. The Committee feels very strongly about this and believes it will be a proper step."

At the request of Dr. O. H. Perry Pepper, Dr. Walter L. Bierring, Chairman of the American Board of Internal Medicine, stated that the adoption of the proposed regulation by the College would not conflict in any manner with the age or time limitations already prescribed in the By-Laws of the College, or those of the American Board of Internal Medicine.

Dr. Pepper pointed out that it is planned to republish the requirements for certification by the American Board of Internal Medicine, because the rules are now read differently by some than by others. He proposed that the Credentials Committee of the College and the By-Laws Committee of the Board might well discuss the matter together and have the proposed action correlated.

Dr. James B. Herrick proposed that final action might be deferred until the next meeting of the Regents, and President Kerr asked the Credentials Committee to confer with the Board of Internal Medicine and re-present the question in December, 1939.

Dr. Sydney R. Miller, continuing his report, pointed out that the Credentials Committee, in preparation for the revision of the informative booklet concerning requirements, send a copy of the booklet with a letter to every Regent and Governor, requesting a careful study and making suggestions for constructive changes to be considered and consolidated by the Committee. He pointed out that this might serve as a wide basis of opinion on which to base not only the changes suggested, but perhaps, other revisions.

Dr. David P. Barr, Chairman of the Committee on Fellowships and Awards, reported that Dr. Jonathan C. Meakins had recommended that inasmuch as Dr. Kenneth Austin Evelyn desired to pursue a further year as an Assistant Resident, the Research Fellowship awarded him as of July 1, 1939, be delayed until July 1, 1940. Dr. Barr recommended that the Research Fellowship be so delayed.

On motion by Dr. Barr, seconded by Dr. O. H. Perry Pepper, and regularly carried, it was

RESOLVED, that the Research Fellowship awarded Dr. Kenneth Austin Evelyn, at his request, be delayed until July 1, 1940.

Dr. Walter L. Bierring made the following report for the American Board of Internal Medicine:

"On behalf of the American Board of Internal Medicine, I wish to give only a brief report, a report of progress in the methods and procedure of certification. Certification without examination is gradually becoming limited to very exceptional cases. Certification by examination is comprising a larger group of applications. In the written section examinations held in October and February, two hundred and sixty-five appeared for examination at different centers throughout the country and Canada. Failures comprised approximately 15 per cent. There appeared in this Session the largest number of candidates for a practical examination, 75, and of these, 19 failed; 20 or 25 per cent. Certain changes are being made in the requirements, and it is hoped that there may also be a coördination with the requirements of this College and other certifying boards or agencies. There have been some changes in the official family. Dr. Ernest E. Irons has been selected as Chairman, Dr. Reginald Fitz as Vice-Chairman and Dr. William S. Middleton as Secretary."

On motion by Dr. Bierring, seconded by Dr. O. H. Perry Pepper, and regularly carried, it was

RESOLVED, that the Board of Regents of the American College of Physicians shall reappoint Dr. David P. Barr to succeed himself as a representative of this College on the American Board of Internal Medicine for the term expiring 1942.

On inquiry from Dr. Sydney R. Miller, Dr. Walter L. Bierring explained that if a candidate fails in the written examination he cannot appear for reëxamination for a period of two years; if failing in the practical examination, he may re-appear in one year.

Dr. James Alex. Miller, Chairman of the Committee on Finance, reported as follows: "This is the report of the Committee which was appointed at the December, 1938, meeting of the Regents to consider dues and initiation fees. I was appointed Chairman of a special Committee with power to select other members. Dr. Paullin and Dr. Stroud served as the other members. This Committee has reviewed with care the statement of income and analyzed its sources, showing that approximately 35 per cent of the College income is from dues and 17 per cent is from initiation fees. Both dues and initiation fees have been reduced 25 per cent in recent years. The various projects proposed by the College, both for the future and in operation at present, lead the Committee to recommend that there be no change in dues at this time, but the Committee also recommends to the Board of Regents that it authorize, through a suitable committee, a careful study of our income and expenditures, both as they exist at present and particularly as to how they should be planned for the future, and that the factors above enumerated, as well as others that will undoubtedly suggest themselves, be considered by such a committee, and that a report be rendered to the Board of Regents."

On motion by Dr. James Alex. Miller, seconded and regularly carried, the above report was accepted.

In further commenting on the resolution above adopted, Dr. James Alex. Miller pointed out that an analysis as proposed will involve matters under the jurisdiction of various committees, such as the Committee on Exhibits and Advertisements, Committee on Future Policy, the Committee on Fellowships and Awards and the Committee on Postgraduate Education. He pointed out that there are many items that need

review, not simply by the Finance Committee, but by all the factors which are represented here, which have to do particularly with future policies. There has been some discussion of altering the commercial exhibits, from which we have received a net profit varying from six to fourteen thousand dollars, according to the place of meeting. He pointed out also that there has been an increasing amount of expenditures for the annual meetings; that there have been suggestions for an increase in the Endowment Fund. Dr. Miller felt that these issues should be intelligently and intensively studied. He recommended that the President and the President-Elect will bear in mind the appointment of those who are capable of facing this whole question of the financial future, from the standpoint of these considerations.

On further motion by Dr. James Alex. Miller, seconded and regularly carried, it was

RESOLVED, that the action taken at the last meeting of the Board of Regents be rescinded in respect to a committee to confer with the Committee on Commercial Exhibits, and that the special committee of investigation be authorized to act in this capacity.

The special committee of investigation of fees and dues was discharged with the thanks of the College.

President Kerr brought up the matter of the joint meeting between the College and the American Medical Association, and reported that Secretary Olin West of the American Medical Association had suggested the possibility of the meeting being held on the last Saturday in April, between the Regents of the College and the Trustees of the American Medical Association.

Dr. Kerr reported that he had discussed with Dr. West the question of other problems that Dr. West had proposed for discussion, and had told him that this College would not feel we were prepared to take up economic or other problems outside of the field of graduate or postgraduate education. Dr. West had stated that he would bring this to the attention of the Board of Trustees, and assured Dr. Kerr that the subject of postgraduate training would be the chief topic of discussion.

Dr. O. H. Perry Pepper recommended that the so-called Liaison Committee, which had been appointed some years ago to confer with a similar committee of the American College of Surgeons, he suspended, because it does not serve as an executive committee and also because the College already has a multiplicity of committees, the duties of which are not well defined. Dr. Pepper suggested that more responsibility might properly be turned over to the present Executive Committee, and thus simplify our structure.

President Kerr, pointing out that the Liaison Committee is not an official committee, declared it suspended.

The Secretary, Mr. Loveland, presented a list of six Associates and five Fellows, whose dues were delinquent two or more years, and who, according to the By-Laws, should be dropped from the Roster. The list had been presented to the Board of Governors for review, so that each Governor might have an opportunity to make suggestions or recommendations.

On motion by Dr. Barr, seconded by Dr. Paullin, and regularly carried, it was

RESOLVED, that the delinquent Fellows and Associates shall be dropped from the Roster of the College at the end of sixty days from this meeting, unless they shall have in the meantime satisfied the provisions of the By-Laws with regard to payment of their dues.

The Secretary, Mr. Loveland, then presented the list of Associates elected at the 1934 Annual Session, whose maximum five-year term had expired without their

meeting the requirements for Fellowship. An analysis of the 1934 class of Associates showed the following results:

Advanced to Fellowship	79	(82.3%)
Credentials not presented	11	(11.5%)
Credentials presented, but inadequate for election	3	(3.1%)
Previously dropped or resigned	3	(3.1%)
Total, Associates elected, 1934	96	

In accordance with the By-Laws, those Associates who had not presented their credentials, or credentials had been found inadequate, totalling 14, were discontinued on the Associateship Roster.

The Secretary, Mr. Loveland, presented an inquiry from the College Governor for Florida, Dr. Turner Z. Cason, concerning the presentation of candidates for membership from Cuba. Dr. Cason, if authorized by the Board of Regents, would endorse these candidates for membership, but unfortunately they were not acquainted or connected in the United States, and have no acquaintanceships among Fellows of the College who may act as their proposers and seconders.

In the discussion that followed, it was brought out that the College has previously gone on record as not encouraging the proposal of candidates from any country unless they speak English, and thus may receive some direct benefits through the journal, the Annual Sessions and other activities of the College. It was further brought out that there would be an undue responsibility given to the Credentials Committee to select the pioneer members of the College from the Island of Cuba, if these men shall be totally unknown to any who are already Fellows of the College.

On motion by Dr. Pincoffs, seconded by Dr. Paullin, it was

RESOLVED, that there be no special action setting aside the present provisions of the By-Laws to enable candidates from Cuba to be presented for membership.

Dr. Charles H. Cocke, Chairman of the Board of Governors, reported upon the proceedings of that body at its meeting on March 27, including: (1) discussion of the question of commercial exhibits, responsibility for which rests in the hands of a Committee appointed by the Board of Regents; (2) Governor Henry M. Thomas, Jr., of Maryland, had suggested that the Board of Regents appoint a committee or director to supervise, organize and correlate the postgraduate courses offered by the College, so that scheduled courses shall not be dropped in the future; further that this committee shall collect data to find out the wishes of the membership with regard to courses desired, suitable time of the year, etc. Dr. Cocke had suggested to individual Governors that they canvass members in their territory who attended the various postgraduate courses of the College, after the list has been furnished by the Executive Secretary, in an attempt to secure such additional information. The findings of the Governors will be submitted to the Committee on Postgraduate Education. The question of location of courses, the Governors felt, should be carefully studied, because it plays such an important part in the popularity of courses; (3) the Governors felt it important that announcement of time and place of postgraduate courses should be made early, so that members may make plans, financially and professionally, in time to attend.

Dr. O. H. Perry Pepper suggested that the Board of Governors may be the best agency through which to appoint a committee for this investigation, the Governors being closer to the membership.

On motion by Dr. Pepper, seconded and regularly carried, it was

RESOLVED, that the Board of Regents request the Board of Governors to appoint a committee or chairman for the purpose of carrying out investigation of the postgraduate courses as they deem best.

Dr. Pepper pointed out, after the adoption of the motion, that this new committee will merely be an advisory committee to furnish data to the present Committee on Postgraduate Education.

Dr. O. H. Perry Pepper reported that on the list of the Board of Directors of the Gorgas Memorial Institute, the name of Dr. James H. Means appears as a representative of the American College of Physicians. Dr. Pepper had been notified that his name would appear on the next list. Dr. Pepper asked the Board if the College desires to be represented. Such representation implies responsibility and approval of that body.

On motion by Dr. Pepper, seconded and regularly carried, it was

RESOLVED, that the question as to whether the American College of Physicians shall be officially represented on the Board of Directors of the Gorgas Memorial Institute shall be left over for consideration at a later meeting.

DR. WILLIAM J. KERR: "I should like to say that this is the last meeting of the Board of Regents over which I shall preside, and I want to take this opportunity to thank you all for the opportunity to work with you and to work on the program and do the other things pertaining to the office. I am glad I had a year of preparation for this, but the year just coming to a close has been of tremendous interest and of educational value to me, and I am grateful for the honor and opportunity. There is something else very close to my heart. I notice, in plans to come before the College on Thursday, recommendations of the Nominating Committee, following the rules of the College, indicate that there are certain ones who have been with us a great many years, the names of which will no longer be on the active list of Officers or Regents. Four of our most distinguished men in American medicine will no longer be on this list. Dr. Pottenger, particularly, has been on the Board longer than anyone else. Dr. Herrick, Dr. Bierring and Dr. James Alex. Miller have been on many years, and have given excellent and remarkable service, and I think that the College is losing from its active list the remarkable work of these men, although I know we shall always be able to turn to them for help and advice. When we adjourn today, we do so in affection to these men."

Adjournment:

Attest: E. R. LOVELAND,
Executive Secretary

MINUTES OF THE BOARD OF REGENTS

New Orleans, La., March 31, 1939

The third meeting of the Board of Regents, held in connection with the Twenty-third Annual Session of the College, was called to order on March 31, 1939, at the Municipal Auditorium, New Orleans, La., with the newly inducted President, Dr. O. H. Perry Pepper, presiding, with Mr. E. R. Loveland acting as secretary, and with the following present:

O. H. Perry Pepper, *President*
William D. Stroud, *Treasurer*
George Morris Piersol, *Secretary-General*
Ernest B. Bradley
Robert A. Cooke
D. Sclater Lewis
Hugh J. Morgan
Francis G. Blake
William J. Kerr

Charles T. Stone
Maurice C. Pincoffs
Charles H. Cocke

The secretary read abstracted Minutes of the preceding meeting of the Board of Regents, which were approved as read.

The Secretary was called upon to present invitations for the 1940 Session of the College. For 1940 he presented invitations from Rochester, N. Y.; San Francisco, Calif.; St. Paul. Minn.; Buffalo, N. Y.; Cleveland, Ohio and Boston, Mass. For 1941, he presented an invitation from Kansas City, Mo. The invitations from Rochester and Buffalo were primarily civic ones, coming from the local Chambers of Commerce. The interest of the Board was primarily focused, for geographic reasons, on the invitations from Cleveland and Boston, and, therefore, these invitations were read in detail. They included official letters not only from the civic bodies, but from the Deans of the Medical Schools, the local medical societies, civic authorities, and others. Dr. William J. Kerr explained that the invitation from San Francisco would be continued for the future, and he withdrew the invitation for current consideration. Inasmuch as Dr. Vernon Rowland and Mr. Mark Egan were present as representatives from Cleveland, they were called upon to present in more detail the facilities available.

Dr. Vernon Rowland: "As a representative of the Cleveland profession and the Academy of Medicine, I am authorized to extend a cordial and official invitation from Cleveland. It has been twelve years since the College met there. Cleveland's renewed invitation was in last year, and there has been increasing interest since then. You are already familiar with the Lakeside Hospital group in Cleveland; its staff will give full coöperation, as will also that of the Children's Hospital. We have a large City Hospital with over three thousand beds, with all branches of service. There is a tuberculosis and chest surgery clinic. Also, there are a group of private hospitals. The American Medical Association will convene in Cleveland in 1941, and since the College meeting is overdue, we think 1940 would be the right time for this meeting in Cleveland. We have all the physical equipment necessary. There is a new public hall for the exhibits and the General Sessions. Its music hall, seating three thousand, is very popular, artistic and acoustically perfect. There are facilities for round tables and small group meetings. The public hall is offered free of all charge to the College; in addition, the services of the Convention Bureau and their corps of helpers, as well as free time on the radio, if desired, will be available. The auditorium is within walking distance from the downtown hotels.

"There are adequate hotel facilities, and I can guarantee eight or nine hundred rooms, or more, at the time of the College meeting. The Cleveland Hotel is under the same roof as the Terminal Station, which is the center of transportation. It has a huge garage, and is almost a town in itself. The Statler Hotel is also located within walking distance of the auditorium, and offers splendid facilities.

"As to location, Cleveland is centrally located, and on all transportation lines. In general, we think we have the clinical facilities and physical equipment necessary, and we believe wide interest and full coöperation will be at your disposal. It would be particularly timely for the College to come to Cleveland in 1940, as the American Medical Association will meet there in 1941. We feel your meeting with us is overdue. I wish to assure you that if the Board decides to accept this invitation, Cleveland will give its best efforts and time."

Mr. Mark Egan: "Mr. President and members of the Board of Regents, I have nothing to add particularly, but I did want to be here to let you know that we mean to coöperate with your headquarters and your local committees. I think Dr. Rowland has mentioned everything, unless you have questions to ask. We can furnish a fine place for exhibits, and we call your attention to the fact that you will be able to

proceed to the meeting rooms from the exhibit hall. There are eight meeting rooms under one roof, and ample meeting facilities."

Answering an inquiry by Dr. Charles H. Cocke, Dr. Rowland stated that the most appropriate dates would be the last week in March or the first week in April, 1940, both of these dates being open.

President Pepper then called upon Dr. James H. Means to submit the invitation from Boston.

DR. JAMES H. MEANS: "Mr. President, I have come here at your invitation. I am authorized to speak for no one but myself. You already have the letters of invitation from our Boston institutions and organizations. I shall be glad to answer any questions; I can speak for my own clinic, saying that we shall be happy to entertain the members of the College in 1940, or any other year. I spent a day with the Executive Secretary looking over the facilities in Boston. They are nothing like they are in Cleveland, but the clinical facilities are good. We have medical schools and a number of hospitals, and all of these, I am sure, would like for you to come to Boston. There are two Regents and one Governor from Boston, each of whom has joined the invitation."

On inquiry by Dr. Pincoffs, Dr. Means replied that while Boston would prefer having the College in 1940, it would welcome the College in 1941 or any other year.

President Pepper thanked Dr. Means, Dr. Rowland and Mr. Egan for coming and presenting the invitations, but said that discussion and decision would be deferred until later on the agenda, whereupon Drs. Means and Rowland and Mr. Egan retired.

Dr. William J. Kerr reported that he had exchanged telegrams with Dr. Olin West of the American Medical Association concerning the joint meeting of our Regents and the American Medical Association Trustees.

On motion by Dr. Kerr, seconded by Dr. Charles T. Stone, and regularly carried it was

RESOLVED, that the full Board of Regents of the American College of Physicians accept the invitation of the Trustees of the American Medical Association to hold a joint meeting at the American Medical Association's headquarters in Chicago on Saturday, April 29; further RESOLVED, that the necessary expenses of the Regents for attendance at this meeting shall be borne by the College.

It was pointed out that our Board of Regents may hold a meeting of its own at the Drake Hotel, Chicago, after the joint session with the Trustees of the American Medical Association is over. Details were left to the Executive Secretary and the President.

The next order of business concerned a decision as to whether the College should have representation on the Advisory Council on Education, Licensure and Hospitals.

DR. HUGH J. MORGAN: "Mr. Chairman, the Committee on Postgraduate Education recommends that the College approve the formation of this Advisory Council, and shall appoint two representatives from the College, these representatives to be instructed to bring before the Council our problems in postgraduate training for discussion and for such advice as this Council will deem wise to give. I think it would be a logical thing for the College to have such representation, if this Council is coming into being. There is no doubt that interested organizations are going to join this Council. The idea of such a Council is a reasonable and sound one, and I think no harm will be done by attempts that this Council may make in the field of graduate education."

On motion by Dr. Morgan, seconded by Dr. William D. Stroud, and regularly carried, it was

RESOLVED, that the American College of Physicians shall accept the invitation to appoint two representatives on the Advisory Council on Medical Education, Licensure and Hospitals, and that these two representatives shall be appointed by the President.

Thereafter, President Pepper appointed as the College representatives, Dr. Hugh J. Morgan and Dr. James H. Means.

The next order of business was the election of the Treasurer, Secretary-General, Executive Committee and the appointment of other standing committees.

On motion by Dr. M. C. Pincoffs, seconded by Dr. William J. Kerr, and unanimously carried, Dr. William D. Stroud was reëlected as Treasurer of the College.

On motion by Dr. Charles H. Cocke, seconded by Dr. Ernest B. Bradley, and unanimously carried, Dr. George Morris Piersol was reëlected Secretary-General.

For the Executive Committee, Dr. M. C. Pincoffs nominated Dr. Reginald Fitz; Dr. George Morris Piersol nominated for reëlection Dr. Roger I. Lee, Dr. Hugh J. Morgan and Dr. M. C. Pincoffs. The nominations were seconded by Dr. William D. Stroud. Dr. George Morris Piersol nominated Dr. Ernest B. Bradley, the motion being seconded by Dr. Charles H. Cocke. A motion was made, seconded and carried that the nominations be closed, and that the secretary cast the ballot; therefore, the personnel of the Executive Committee for 1939–40, the President, President-Elect, Treasurer and Secretary-General being members ex officio, consists of the following:

EXECUTIVE COMMITTEE, 1939–40

O. H. Perry Pepper, *Chairman*
James D. Bruce
George Morris Piersol
William D. Stroud
Ernest B. Bradley
Reginald Fitz
Roger I. Lee
Hugh J. Morgan
Maurice C. Pincoffs

On motion by Dr. William J. Kerr, seconded by Dr. Charles H. Cocke, and regularly carried, Dr. Sydney R. Miller was re-nominated as a member of the Committee on Credentials from the Board of Regents for an additional year, until 1940, to coincide with his term as a Regent. President Pepper requested Dr. Miller to continue serving as Chairman of the Credentials Committee.

Dr. Charles H. Cocke, Chairman of the Board of Governors, reported that Dr. J. Owsley Manier, of Nashville, had been reappointed on the Committee on Credentials for the term ending 1942. The full personnel of the Committee on Credentials for 1939–40 is as follows:

COMMITTEE ON CREDENTIALS, 1939–40

Sydney R. Miller, *Chairman*	(1940)	—from the Board of Regents
George Morris Piersol	(1940)	
Ernest B. Bradley	(1941)	
J. Owsley Manier	(1942)	—from the Board of Governors
William B. Breed	(1940)	
Charles H. Cocke	(1941)	

President Pepper reported that according to rules and regulations of the Board of Regents, it was the President's duty to appoint members of several committees,

list of which he read. Before making any appointments, he opened discussion as to the advisability of continuing the present Committee on Future Policy for the Development of Internal Medicine, which has been in existence since 1936. He pointed out that the duties of a new investigative committee very closely duplicate the duties of the Committee on Future Policy.

After general discussion and review of the work of the Committee on Future Policy, Dr. William D. Stroud moved, and Dr. Ernest B. Bradley seconded the motion as follows, which motion was regularly adopted:

RESOLVED, that the present Committee on Future Policy be abolished with thanks, and that the President be empowered to appoint a Special Committee on Survey and Future Policy, consisting of five members to be appointed annually by the President for one year, these members not necessarily selected from the Board of Regents.

In further discussion, it was suggested that this Special Committee on Survey and Future Policy be composed of the Chairmen of several of the more important Committees, such as the Finance Committee, Committee on Credentials, the Editor, the Committee on Exhibits and Advertising and the American Board of Internal Medicine.

President Pepper called to the attention of the Regents that according to the regulations, the Regents appointed the members of only two committees, while the President appoints the members of eleven committees. Some of these committees are appointed without limit; some for one year and some for more than one year; furthermore, that the original motions are not specific as to whether committee members shall be appointed from the Board of Regents or from the membership-at-large, and that frequently appointments from the Board of Regents for terms of two or more years may extend beyond a Regent's term on the Board. In many ways, Dr. Pepper thought it desirable to make use of the Regents and Governors and members-at-large on the committees, and suggested the possibility of a study of committee structure before the next autumn meeting of the Board. He suggested that the Executive Secretary and the President make a study of the situation and draw up some suggestions in this regard.

On motion by Dr. Ernest B. Bradley, seconded by Dr. William D. Stroud, and regularly carried, it was

RESOLVED, that the President be instructed to report at the next autumn meeting recommendations on the qualifications, personnel and tenure of office of committees.

President Pepper reported that he had received the resignation of Dr. Walter E. Vest as Governor for West Virginia. In accordance with the By-Laws, President Pepper appointed to succeed Dr. Vest, Dr. Albert H. Hoge, of Bluefield, W. Va., to serve until the next regular election.

On motion by Dr. Charles H. Cocke, seconded and regularly carried, it was

RESOLVED, that the regrets of the Board of Regents be sent to Dr. Walter E. Vest.

The next order of business was final action on the 1940 meeting place, and President Pepper requested the Executive Secretary to report upon his inspection trips to Boston and to Cleveland.

Mr. Loveland in his report pointed out that in company with Dr. Means, he had recently inspected all possible places for the meeting in Boston, but that none of the halls seemed entirely acceptable, with the result that if the Annual Session of the College shall be held in Boston, it would have to be held in the Statler Hotel. While this hotel has better facilities for the meeting of the College than other places in Boston, it nevertheless had the limitations of a ballroom that would seat not more than fifteen hundred individuals, and very limited space for the exhibits. Space for

round tables would be limited to three rooms a day, with a maximum attendance from 100 to 125 in each. Boston's clinical facilities were excellent; its physical facilities limited.

Mr. Loveland reported that Cleveland has a public auditorium with excellent physical arrangements for the meetings, exhibits, round tables and other features. Both cities have adequate hotel accommodations for as many as would be attending the College Session.

Mr. Loveland also reported that the Board of Governors had unanimously adopted a resolution recommending to the Board of Regents that Cleveland's invitation be accepted for 1940.

The conditions existing in both Boston and Cleveland were discussed at length, whereupon Dr. Hugh J. Morgan moved and Dr. William J. Kerr seconded the following resolution, which was unanimously passed:

RESOLVED, that the 1940 Annual Session of the College shall be held in Cleveland.

Thereafter followed discussion of the appointment of a General Chairman. On motion by Dr. Piersol, seconded by Dr. Cocke, and unanimously carried, it was

RESOLVED, that Dr. Howard T. Karsner, of Cleveland, be elected General Chairman of the 1940 Session.

On motion by Dr. Bradley, seconded and regularly carried, it was

RESOLVED, that the selection of the date of the 1940 Session be left to the President, General Chairman and Executive Secretary.

Dr. Charles H. Cocke reported from the Board of Governors the personnel of that Board's Committee to undertake the investigation and survey of postgraduate courses as follows:

*Dr. Henry M. Thomas, Jr., Baltimore, Md.
Dr. Edward L. Bortz, Philadelphia, Pa.
Dr. James G. Carr, Chicago, Ill.
Dr. James J. Waring, Denver, Colo.
Dr. Ernest H. Falconer, San Francisco, Calif.

On motion by Dr. Hugh J. Morgan, seconded and regularly carried, it was

RESOLVED, that the Executive Secretary express the great appreciation of the College, through the Regents, to all those who participated in arranging and carrying out the Postgraduate Courses in various cities preceding the New Orleans Session.

Dr. Maurice C. Pincoffs made the following suggestions in connection with meetings of the Board of Regents:

(1) that the Board of Regents, following each Regents' meeting, receive a mimeographed copy of the full Minutes;
(2) in advance of each meeting of the Board of Regents, a brief synopsis of the main agenda of the forthcoming meeting be sent to each Regent, so that he may give topics some preliminary thought and consideration;
(3) when a topic of major importance is coming up, a special meeting of the Regents should be held with that as the only topic, rather than having any time given over to routine matters.

Dr. Hugh J. Morgan reported that the American College of Surgeons one year ago had invited the American College of Physicians to work in the field of graduate education. No action had yet been taken in regard to that invitation; and, as the Col-

* Chairman.

lege of Surgeons had been informed that action had been deferred previously, they were looking to this meeting for a decision.

Inasmuch as the Regents had decided to defer action still further, Dr. Morgan proposed that it might be appropriate for our President to write to the American College of Surgeons, informing them that action has been deferred, and that our College is going into the Advisory Council on Medical Education, Licensure and Hospitals to discuss this matter further.

President Pepper expressed the opinion that it is unfortunate that some matters of the greatest importance are left to the Friday meeting of the Board of Regents at the Annual Sessions. These meetings are more sparsely attended than those earlier in the week. He, therefore, suggested that more important matters be scheduled for preliminary discussion and action earlier in the week, probably at the Tuesday meeting. He suggested that instead of scheduling the midweek meeting of the Regents at the noon hour, that a regular morning or afternoon be set aside, so that all important business could be attended to earlier in the week. He felt that members of the Board could sacrifice their scientific interest in the program for that period, and that those making the program should list none of the Regents for the morning or afternoon of this important meeting.

President Pepper announced his appointments to standing and special committees for 1939–40. A list of these committees and members thereof appears in the May, 1939, issue of this journal.

Adjournment:

Attest: E. R. LOVELAND,
Executive Secretary

MINUTES OF THE GENERAL BUSINESS MEETING

New Orleans, La., March 30, 1939

The Annual Business Meeting of Fellows and Masters of the American College of Physicians was held in the Municipal Auditorium, New Orleans, at 4:45 p.m., March 30, 1939, with the President, Dr. William J. Kerr, presiding and the Executive Secretary, Mr. E. R. Loveland, acting as Secretary.

The Minutes of the preceding Annual Business Meeting were read by the Secretary and approved.

President Kerr reviewed the activities of the College during the past year, referring especially to the increase in the diversity of the activities as each year passes. He pointed out that this has given evidence of more specific purpose in the activities of the College and that the initiation of Postgraduate Courses had been of considerable significance. The College had been actively studying the possibility of developing more work in graduate education for men planning to enter the special fields of medicine. He prophesied an extension of the activities of the College in the future and complimented the work accomplished in the executive offices of the College. He extended his appreciation to the Officers, Committees, Regents and Governors, and the Credentials Committee in particular, for the remarkable work they had done during the year. He expressed pleasure in working with Dr. John H. Musser, General Chairman of the New Orleans meeting, in connection with the Twenty-third Annual Session. An effort had been made to bring before the College the very best that could be obtained from all parts of the United States, Canada and Mexico. Approximately three hundred and fifty titles and speakers had been made available on the program, through the General Sessions, Special Lectures, Round Tables, Dry Clinics and hospital Clinics.

In the absence of Dr. William D. Stroud, Treasurer, President Kerr announced that the finances of the College were in excellent shape, that the Finance Committee and the Treasurer had been diligent in their work, and that full details of the Treasurer's annual report would appear in the "Annals of Internal Medicine."

Mr. E. R. Loveland presented the following annual report of the Executive Secretary:

"The proceedings of this meeting, especially those of the Board of Governors and Board of Regents, will be published in the 'Annals of Internal Medicine.' The meeting city for 1940 will be determined by the Board of Regents at its meeting tomorrow. The invitations most seriously under consideration come from Boston and Cleveland.

"The College accounts, according to our universal custom, have been audited by a certified public accountant, and all the statements have been presented and approved by the Finance Committee and the Board of Regents. Through the coöperation of the President, of the Treasurer and of the Secretary-General, as well as other Officers, Regents and Governors of the College, and with the help of a competent staff, the work in the Executive Offices of the College has been carried on with as great dispatch, promptness and efficiency as possible. The Board of Regents authorized the appointment of an assistant to the Executive Secretary at its meeting in December, 1938, and thereafter in consultation with the President-Elect, Secretary-General and the Treasurer, Mr. Lee Russell Hegland was appointed early in February. Mr. Hegland is a graduate of the Wharton School of the University of Pennsylvania and has had a number of years experience before joining our staff. The annual amount of correspondence and details of the Executive Offices has made it utterly impossible

for your Executive Secretary to carry on without assistance. This help and consideration extended by the Regents has been deeply appreciated. It is the aim of your Executive Offices to extend every help and every possible courtesy to the members at all times. We have splendid facilities at our headquarters in Philadelphia, and we wish again to remind you that you are always welcome to visit us.

"The Twenty-third Annual Session of the College in New Orleans has been a most successful and well attended meeting. The President, the General Chairman, the local committees through their chairman, the Convention Bureau, the hotels, the Auditorium staff and the Ladies' Entertainment Committee have done an excellent job, and we appreciate the coöperation and assistance they have given us. Our general registration was 1,574 with 571 visiting ladies, making a total of 2,145."

Dr. George Morris Piersol presented the following annual report of the Secretary-General:

DR. PIERSOL: "Since the last Annual Session of this College, the membership report shows that only five Fellows and three Associates have been dropped for delinquency; the resignations of three Fellows and three Associates have been accepted; four Associates and twenty-nine Fellows have been lost by death; and twenty-two Associates were dropped for failure to qualify for Fellowship in the maximum five-year period, as prescribed by the By-Laws. This year 228 were elected to Fellowship, the vast majority of whom were advancements from Associateship. 204 have been elected to Associateship.

"Sixteen Fellows have become Life Members since the last Annual Session, making a total of one hundred and seventeen on the Life Membership scroll. Eight of these Life Members are deceased, leaving one hundred and nine.

"The total membership of the College is now constituted as follows:

Masters	2
Fellows	3,027
Associates	1,202
	4,231 TOTAL

"The Committee on Postgraduate Education arranged a number of intensive postgraduate courses immediately preceding the opening of this Session. Admission to the courses was restricted to members of the College and those attempting to qualify for membership or for advancement to Fellowship. Two courses were given at Johns Hopkins University and the University of Maryland at Baltimore, one in General Medicine and one in Cardiovascular and Respiratory Diseases. One course was given at Northwestern University, Chicago, in Cardio-Renal-Vascular Medicine; two courses were given at Washington University, St. Louis, one in Cardiovascular Diseases and one in Diseases of the Glands of Internal Secretion. The total registration for these courses numbered about 125, the registrants coming from various parts of the United States and Canada. It is hoped that with the further coöperation of the Governors, this important activity of the College will continue to increase in interest and scope."

DR. PIERSOL: "Mr. President, in the past year, during which you have so ably and wisely guided the destiny of this College, you have become more than ever endeared to all who have had the privilege of working with you. We are deeply appreciative of the never-failing spirit of coöperation and courtesy that has marked all our associations.

"Therefore, on behalf of the Officers, Regents and Governors of the American College of Physicians, I have the honor to present you with this Gavel, an enduring

symbol of the high office which you have held, as well as a token of our affection and esteem."

DR. KERR: "Dr. Piersol, Fellows and Associates, I cannot say that I did not know there was going to be a Gavel presented because I have, upon previous occasions, seen this same thing done, but not until two years ago, on a similar platform, did I have the slightest idea I would be the recipient of such a Gavel. I would like to say only this; that I never have enjoyed two years more in anything I have done in association with my colleagues in this country, and I am very grateful for the honor you have done me. The fellowship in this organization is something superior and I believe it is leading American medicine in the right direction. I thank you from the bottom of my heart.

"It now gives me the very greatest of pleasure to ask two of our distinguished Officers and Fellows to escort the new President to the platform. I am going to ask Dr. Morris Piersol, from the great city of Brotherly Love, Philadelphia, and my fellow Californian, Dr. Francis Pottenger, to escort Dr. Pepper to the platform.

"Dr. Pepper, the destinies of the College are in your hands."

DR. O. H. PERRY PEPPER: "Mr. Chairman, Fellows and Associates, it is hard to believe that two years have passed since I attended the ceremony at which the same thing that is happening to me, happened to Dr. Kerr. It has been very instructive and interesting to watch the College grow under Dr. Kerr's leadership. I can only hope that two years from now I can retire with as clear a conscience.

"The Presidency of the American College of Physicians is a great honor and I assure you that I deeply appreciate it and I shall strive to do all within my power to serve the College faithfully and efficiently, and to continue the successful administration of Dr. Kerr.

"The Officers of the College, its Regents and Governors are merely representatives of the membership, chosen directly or indirectly, to act as a machinery to carry on the business and government of the College, just as Congress does that of the nation.

"There is, however, one great difference—we, the Officers of the College,—receive no mandate on any subject. We did no electioneering and so had no platform and made no promises—possible or impossible.

"This leaves us, of course, freer than Congressmen to do what we think is right, but it also makes it harder for us to know just what our constituents want us to do and we have to decide ourselves what is best for the College.

"In doing this, we need your help; we need the expression of your opinion. And it seems to me that district meetings, such as the very successful one recently held in Philadelphia, under the leadership of Governor Bortz, in addition to being pleasant and useful occasions, offer an excellent opportunity for a free discussion of the activities and objectives of our College; the conclusions being later reported by the Governor to the Board of Governors and Board of Regents. Do you want the College to reduce its activities and cut the dues? Do you want to embark on new activities which might demand more funds? Some of the suggestions which have reached me have certainly fallen into this latter class—for example, the survey of hospitals for internships, residencies and graduate training, or again a survey of public health facilities in the cities of this country.

"Or should we merely increase our present activities as finances and opportunity permit? Should we study the problem of tuberculosis in medical students and interns? Should we try to reduce the cost of medical textbooks? Should we start a golf tournament at our meetings? These latter are mentioned merely to stress the fact that there is nothing that you may not want to discuss.

"But before you crystallize your views concerning the activities and objectives

of the College, you should have clearly in mind the facts of the case, so that you will not be making suggestions which are beyond the possibilities of the College as it now exists. Let me point out that our College is still very young. Like the young, it is tempted to admire and to try to emulate the older and bigger boys.

"Our College has a membership of about 4,200, including Fellows and Associates; the College of Surgeons has over 13,000 Fellows alone; the American Medical Association over 100,000.

"Our College has a gross annual income of about $90,000.00; the College of Surgeons has almost five times as much; while the American Medical Association has a profit from its journal alone about seven times greater than our gross income.

"Our dues are $15.00, our initiation fee, $80.00; the College of Surgeons' dues are $25.00 a year, with an initiation fee of $100.00. Our members receive the 'Annals' free, but the Fellows of the American College of Surgeons have to pay the subscription for 'Surgery, Gynecology and Obstetrics.'

"We are not only young, but still poor and humble. Our headquarters are small and simple, but adequate; only those of you who have seen the buildings of the College of Surgeons and of the American Medical Association can properly compare the three.

"In presenting these comparisons, I am not belittling our College—far to the contrary—for I sincerely admire the steady, healthy growth of our activities during the past years, and it seems to me that the achievements and activities of our College form a very creditable list. Our annual meetings have been increasingly successful and certainly accomplish their purpose of bringing together the pick of the internists of this country and Canada. I can picture no more valuable meeting than ours, with its general sessions, clinics, round table discussions and lectures, not to mention the opportunities for personal exchange of ideas off the meeting floor. I have already mentioned the district meetings, which have been successfully held in several States during the past few years.

"For the past two years, the College has organized the pre-meeting refresher courses, which is another step along the line of offering facilities for graduate education. This is a new activity of the College and may well grow very greatly in the future.

"Next I should mention the journal of the College, the 'Annals of Internal Medicine.' This fine journal has grown steadily to its present size. New departments have been added to it, and there is no reason to think that it will not continue to increase as time goes on and finances make it possible.

"In its meetings and refresher courses and the 'Annals,' the College is encouraging graduate education, and in a small way it is also playing a part in developing graduate training for recent graduates. This year the College granted three Research Fellowships for selected men to continue their work after finishing their internships and commencing their research field. This is graduate training of the best type and is also a contribution towards medical research. The Phillips Award is another item and, as you know, is a reward for research accomplishment. Also, the College has, in coöperation with the American Medical Association, initiated within the past few years the American Board of Internal Medicine, which is another step taken to raise standards of medical practice and to encourage postgraduate training and postgraduate education. Our activities in graduate training are just commencing while the College of Surgeons spends annually in this field alone about as much as our total annual income. Last winter we conferred with the College of Surgeons on these matters; and next month our Regents are to hold a similar meeting with the Trustees of the American Medical Association.

"Now it seems to me that this is a remarkably fine record, and I, as a member of the College, am proud of the record of the College and naturally as an Officer of the College, I am proud to be an Officer, but also I feel deeply the responsibility of

helping to continue the advances which the College has made. However, there is the danger of our College trying to move too fast, trying to undertake too much for its present age, size and income.

"Now obviously the most popular program for a politically minded President to offer is more service and less taxes. Unfortunately, for me, I am so sincerely impressed with what our College has done and is doing today, that I believe our chief need is to move slowly and, as we said in the war, 'to consolidate our position.'

"As institutions go our College is still very young and I for one seldom advise the use of growth hormones in boys who seem perhaps a trifle slow in growth. Usually they go on their normal course and catch up when the puberty spurt of growth takes place. This is a far healthier program for boys, and so it seems to me it is for our College. Let us be ourselves—go our own way, develop our own character and personality. No testosterone for us! Let us admire the College of Surgeons, the American Medical Association, the Association of American Physicians and other organizations, but let us not feel we must copy each of them. Let us respect their several special fields of activity, and leave to them those things that are more appropriate for them than for us.

"In this manner, it seems to me, our College can best serve its members and carry out the purposes for which it was founded as stated in Section I, Article III of our Constitution:

'The object of the American College of Physicians shall be to establish an organization composed of qualified internists of high standing who shall meet from time to time for the purpose of considering and discussing medical and scientific topics, and who through their organization shall attempt to accomplish the further purposes of: (*a*) maintaining and advancing the highest possible standards in medical education, medical practice and clinical research; (*b*) perpetuating the history and best traditions of medicine and medical ethics, and (*c*) maintaining both the dignity and the efficiency of Internal Medicine in its relationship to public welfare.'"

President Pepper called for the report of the Committee on Nominations, which, in the absence of the Chairman, Dr. James Alex. Miller, was presented by Dr. D. Sclater Lewis, a member of this Committee.

DR. LEWIS: "Mr. President, in accordance with the By-Laws, Article I, Section 2, we present the following report of the Nominating Committee:

"(A) *For the Elective Offices:*

President-Elect .....James D. Bruce, Ann Arbor, Mich.
First Vice President .....Allen A. Jones, Buffalo, N. Y.
Second Vice President .....Gerald B. Webb, Colorado Springs, Colo.
Third Vice President .....J. Morrison Hutcheson, Richmond, Va.

This list of nominees has been duly published in the 'ANNALS OF INTERNAL MEDICINE' at least one month before the present date.

"(B) *For the Board of Regents:*

Term Expiring 1942

Charles T. Stone, Galveston, Tex.
Reginald Fitz, Boston, Mass.
Egerton L. Crispin, Los Angeles, Calif.
Francis G. Blake, New Haven, Conn.
William J. Kerr, San Francisco, Calif.

"(C) *For the Board of Governors:*

Term Expiring 1941

Charles H. Turkington .....Connecticut—Litchfield

Term Expiring 1942

Oliver C. Melson .....Arkansas—Little Rock
Ernest H. Falconer .....Northern California—San Francisco
Fred M. Smith .....Iowa—Iowa City
Joseph E. Knighton .....Louisiana—Shreveport
Henry R. Carstens .....Michigan—Detroit
Edgar van Nuys Allen .....Minnesota—Rochester
A. Comingo Griffith .....Missouri—Kansas City
Robert B. Kerr .....New Hampshire—Manchester
George H. Lathrope .....New Jersey—Newark
Charles H. Cocke .....North Carolina—Asheville
Julius O. Arnson .....North Dakota—Bismarck
Alexander M. Burgess .....Rhode Island—Providence
Kenneth M. Lynch .....South Carolina—Charleston
Paul K. French .....Vermont—Burlington
Walter B. Martin .....Virginia—Norfolk
Charles E. Watts .....Washington—Seattle
Walter E. Vest .....West Virginia—Huntington
Hugh A. Farris .....Maritime Provinces—St. John, Canada
Charles F. Moffatt .....Quebec—Montreal, Canada

Respectfully submitted,

Dr. D. Sclater Lewis,
Dr. Henry M. Thomas, Jr.,
Dr. Fred W. Wilkerson,
Dr. Donald J. Frick,
Dr. James Alex. Miller, *Chairman,*
Committee on Nominations"

President Pepper then called for any nominations that might be made from the floor. In the absence of any such nominations from the floor, motion was made, seconded and regularly carried, that it be

Resolved, that nominations be closed and that the Executive Secretary be instructed to cast a unanimous ballot.

The Secretary declared all nominees presented by the Committee on Nominations elected.

At this point, President Pepper requested Dr. Francis M. Pottenger and Dr. George Morris Piersol to conduct to the platform, the President-Elect, Dr. James D. Bruce, Ann Arbor, Michigan.

On motion by Dr. C. W. Dowden, seconded and unanimously carried, it was

Resolved, that the cordial thanks of the American College of Physicians be extended to the Retiring President, Dr. William J. Kerr; to the General Chairman, Dr. John H. Musser; and to the chairmen and members of his various committees, individually and collectively, for their faithful work in the preparation and conduct of the New Orleans Session; to the Ladies Entertainment Committee for their efficiency, hospitality and courteous entertainment of our ladies; to the medical schools and hospitals of New Orleans for putting their facilities at the disposal of the College,

and for their helpful participation; to the New Orleans Association of Commerce and its officers for their assistance; to the New Orleans Municipal Auditorium and its staff for exceptional coöperation and help; to the Roosevelt and Jung Hotels for their assistance and aid in providing for our entertainment and comfort.

On motion by Dr. Allan Eustis, seconded and unanimously carried, it was

RESOLVED, that a special vote of thanks be extended through Mr. Edgar Rea, Manager of the Municipal Auditorium, to all employees under him for their uniform, efficient coöperation during the Convention, and especially to Mr. Bourda for his arrangement of the lighting in the Auditorium.

Adjournment:

Attest: E. R. LOVELAND,
Executive Secretary

THE AMERICAN COLLEGE OF PHYSICIANS

EXECUTIVE SECRETARY'S FINANCIAL REPORT

1938

The Auditor's report of his examination of the accounts of the College is hereto attached. The activities of the College are growing rapidly from year to year, but increased income from the annual exhibits, advertising in the "ANNALS OF INTERNAL MEDICINE" and a gradual growth in membership preserves a satisfactory credit balance, as indicated by a total balance of $16,630.65, of which $4,021.98 was added to the Endowment Fund and $12,600.67 was added to the General Fund.

1935 Balance	$17,182.09	1937 Balance	$23,765.75
1936 "	24,946.53	1938 "	16,630.65

Due to a change in accounting policy, which more clearly sets out the true financial condition of the College, only a proportion of the subscription receipts for Volume XII, "ANNALS OF INTERNAL MEDICINE" (July, 1938, to June, 1939), have been credited to 1938, the balance being reserved to cover expenses of publication of the last six numbers (January to June, 1939) of the journal. During previous years the entire subscription receipts were credited to the current year, and, therefore, to make the 1938 balance comparable with the balances of preceding years above recorded, $13,723.24 should be added to the 1938 figure.

The total principals of the two Funds on December 31, 1938, were:

Endowment Fund	$ 68,564.25
General Fund	153,449.87
	$222,014.12

Although no liquidating dividends were received during 1938 from the banks in Pittsburgh that closed during the depression, and in which there remains a balance of $5,709.33, we are assured of some dividends during 1939. It is probable that the College will never collect the full balance from these closed banks, but it has been totally impossible to determine or estimate what proportion of the balance will eventually be paid.

Attention is called to the recommendation of the Auditor that a proportion of the investments in the General Fund, represented by bonds, be transferred to the Endowment Fund, because it seems improbable that these funds will be required in the General Fund and because these investments are functioning generally as endowment funds already.

Due to materially increased income from subscriptions and advertising in the "ANNALS OF INTERNAL MEDICINE," Volume XI, which was completed with the June, 1938, Issue, showed a surplus of $6,678.86, in spite of the fact that this volume contained about four hundred more pages than any preceding Volume of the journal.

While the expenses for conducting the Twenty-second Annual Session in New York City during 1938 were considerably in excess of those for any preceding meeting, the income from exhibits and guest fees was very much larger than from any preceding meeting, with the result that there was a credit balance of $2,126.88.

Page 14 shows a summary of the budgets approved by the Board of Regents on December 18, 1938, for the year 1939; to wit, a total estimated income of $98,100.00 and total estimated expenditures of $77,875.00, with an estimated balance of $20,225.00.

Respectfully submitted,

(Signed) E. R. LOVELAND,
Executive Secretary

March 1, 1939.

H. I. MACLEAN

309 Valley Road

Llanerch, Pa.

February 28, 1939

To the Board of Regents
American College of Physicians, Inc.
Philadelphia, Pa.

Mr. E. R. Loveland, Executive Secretary

Dear Sirs:

I have examined the accounts of the

AMERICAN COLLEGE OF PHYSICIANS, INC.

for the year ended December 31, 1938, and the accompanying statements, including the Balance Sheet at December 31, 1938, the analyses of the General Fund and the Endowment Fund and the Detailed Statement of Operations for the year ended December 31, 1938, are in accordance with the books of account and in my opinion set forth correctly the financial position at December 31, 1938, and the results of operations for the calendar year ended December 31, 1938, subject to the following comments:

Cash: The cash was properly accounted for. The following is a statement of the cash in the various depositories:

Girard Trust Company, Philadelphia	$6,260.69
Provident Trust Company, Philadelphia	861.47
Royal Bank of Canada, Montreal	1,005.80
	$8,127.96

Accounts Receivable: The accounts receivable were examined and found to be less than one year old and appear to be good and collectible. The detailed accounts receivable were in agreement with the control account. No requests for confirmation of the accounts were mailed.

Investments: The securities were accounted for by direct correspondence and the income for the period under review was verified.

Deferred Claims: The amount of the deferred claims, representing the funds due from the receivers of closed banks is as follows:

	Balance Dec. 31, 1938
Bank of Pittsburgh, Pittsburgh	$1,461.97
Exchange National Bank, Pittsburgh	1,166.14
Highland National Bank, Pittsburgh	3,081.22
	$5,709.33

It is noted that no liquidating dividends were received during 1938, and it is, therefore, suggested that the accounts be reviewed in order to determine the amount that may be paid upon final liquidation and the accounts adjusted accordingly.

General Fund: The book value of the investments of the General Fund at December 31, 1938, amounted to $92,186.30, and it is noted that such investments are held principally for the purpose of yielding income for the College rather than for current operating purposes. Inasmuch as these investments are functioning generally as endowment funds, it is recommended that the College consider the advisability of a transfer from the General Fund to the principal of the Endowment Fund, or to classify such an amount as may not be required for current operations to another classification which may be called Funds Functioning as Endowment. Such an action would enable the current financial position of the College to be more clearly stated.

General: The increase in the amount of the Endowment Fund and the General Fund during the year 1938 is as follows:

	Balance Jan. 1, 1938	*Net Increase*	*Balance Dec. 31, 1938*
Endowment Fund	$ 64,534.27	$ 4,029.98	$ 68,564.25
General Fund	140,849.20	12,600.67	153,449.87
	$205,383.47	$16,630.65	$222,014.12

In accordance with the instructions of the Executive Secretary, the subscription account of Volume XII of the ANNALS OF INTERNAL MEDICINE was adjusted so as to include only the estimated amount of income applicable to the operations for the year based on the number of issues published for which printing costs had been incurred to December 31, 1938. The prepaid insurance at December 31, 1938, was not set up as a deferred expense; the other deferred and accrued items were verified; the charges to the College Headquarters account were examined, and in my opinion appear to be proper charges to this account; the charges to the Furniture and Equipment accounts represent proper additions to this account and the allowance for depreciation appears to be adequate; a depreciation reserve account has been set up for the new building in accordance with the action of the Board of Regents at the meeting on December 12, 1937, which provided that depreciation on the building should be taken into account at the rate of $1,000.00 per year; the footings and extensions of the inventory were verified; in accordance with the action of the Board of Regents at the meeting on December 12, 1937, a reserve fund of $2,000.00 has been set up in order to amortize the cost of the Directory over a two year period; all ascertainable liabilities have been included in the balance sheet; all recorded receipts from dues, initiation fees, exhibits, advertising, sales of publications, etc., were properly deposited in bank and all disbursements, as indicated by the vouchers, cancelled checks and bank statements, were properly recorded in the books of account.

Very truly yours,

(Signed) H. I. MACLEAN,
Certified Public Accountant

AMERICAN COLLEGE OF PHYSICIANS, INC.

Balance Sheet, December 31, 1938

General Fund

Assets			*Liabilities*	
Cash in banks and on hand		$ 7,174.14	Accounts Payable	$ 73.00
Accounts Receivable:			Deferred Income:	
Advertising	$ 818.56		Advance Subscriptions, ANNALS OF INTERNAL MEDICINE	14,270.86
Hornblower and Weeks	37.04	855.60	23rd Annual Session, Exhibit	2,014.69
Inventory of Keys, Pledges and Frames, at cost		439.55	Directory Publication Reserve Fund	2,000.00
Accrued Income on General Fund Investments		592.50		
Accrued Income on Endowment Fund Investments, Due to General Fund		742.70		
Investments at Book Value		92,186.30		
Insurance Deposit		555.00		
Deferred Expenses, 23rd Annual Session		2,611.69		
Deferred Claims:				
Banks in process of liquidation:				
Bank of Pittsburgh	$ 1,461.97			
Exchange National Bank, Pittsburgh	1,166.14			
Highland National Bank, Pittsburgh	3,081.22	5,709.33	General Fund, as annexed	153,449.87
College Headquarters, Real Estate	57,728.45			
Less, Allowance for Depreciation	2,000.00	55,728.45		
Furniture and Equipment, at cost	9,565.85			
Less, Allowance for Depreciation	4,352.69	5,213.16		
		$171,808.42		$171,808.42

Endowment Fund

Cash in Banks		$ 1,153.82	Endowment Fund, Principal	$ 68,564.25
Accrued Interest		742.70	Accrued Income, Due General Fund	742.70
Investments at Book Value		67,410.43		
		$ 69,306.95		$ 69,306.95
TOTAL ASSETS		$241,115.37	TOTAL LIABILITIES AND FUNDS	$241,115.37

General Fund

For the Year Ended December 31, 1938

Balance, January 1, 1938			$140,849.20
Less:			
Transfer to Endowment Fund of the Initiation Fees of Life Members			1,070.00
			$139,779.20
Summary of Operations for the Year ended December 31, 1938:			
Income:			
Annual Dues		$26,339.77	
Initiation Fees		13,925.00	
Subscriptions, Annals of Internal Medicine		12,667.38	
Advertising, Annals of Internal Medicine		9,592.95	
Income from Invested Funds, General		3,063.07	
Income from Invested Funds, Endowment		2,616.65	
Exhibits, 22nd Annual Session		13,442.20	
Guest Fees, 22nd Annual Session		745.00	
Round Tables, net, 22nd Annual Session		196.68	
Profit on Keys, Pledges and Frames		143.21	
Dividend on Perpetual Insurance Deposit		60.00	
Annals of Clinical Medicine		14.60	
Total Income			$82,806.51
Expenses:			
Salaries		$20,854.42	
Postage, Telephone and Telegraph		3,678.99	
Office Supplies and Stationery		1,313.35	
Printing		20,815.29	
Traveling Expenses		4,687.77	
College Headquarters:			
Maintenance	$2,422.83		
Taxes	1,168.75		
Insurance	179.03	3,770.61	
Directory Publication Reserve Fund		2,000.00	
Loss on Sale of Investments, General Fund		2,031.71	
Depreciation on Building, Furniture and Equipment		1,788.42	
Grant to Commission on Graduate Medical Education		100.00	
Postgraduate Courses, net		566.15	
John Phillips Memorial Prize		107.01	
Research Fellowships		3,006.71	
Other Expenses:			
22nd Annual Session	$3,124.24		
Annals of Internal Medicine	439.24		
Miscellaneous	851.93	4,415.41	
Total Expenses			$69,135.84
Net Income for the Year Ended December 31, 1938			13,670.67
Balance, December 31, 1938			$153,449.87

Endowment Fund

For the Year Ended December 31, 1938

Principal Account, January 1, 1938			$64,534.27
Add:			
Life Membership Fees received during 1938		$3,066.00	
Transfer of Initiation Fees of New Life Members from General Fund		1,070.00	4,136.00
			$68,670.27
Deduct:			
Loss on Sale of Investments			106.02
Principal Account, December 31, 1938			$68,564.25
Income Account:			
Income from Investments earned during 1938			$ 2,616.65
Deduct:			
Research Fellowships		$3,006.71	
John Phillips Memorial Prize		107.01	3,113.72
Excess of Expenses over Income, charged to General Fund Operations for 1938			$ 497.07

INVESTMENTS

December 31, 1938

Par Value	*Bonds*	*Endowment Fund Investments*	*General Fund Investments*	
$ 4,000	Appalachian Electric Power Co., Deb., 4½s, 1948	$ 4,140.00		
5,000	Bell Telephone of Canada, 5s, 1955	5,562.50		
2,000	Canadian Nat'l (West Indies) SS. Co., Ltd., 5s, 1955	2,040.00		
5,000	Columbia Gas & Electric Corp., Deb., 5s, 1961		$ 4,956.25	
5,000	Commonwealth Edison Co., 1st Series "F," 4s, 1981	4,744.35		
5,000	Florida Power Corp., 1st Mort., Series "C," 4s, 1966		4,485.90	
5,000	Government of Dominion of Canada, 4s, 1960	4,662.50		
2,000	Great Northern Railway Co., Series "H," 4s, 1946	2,100.45		
3,000	Great Northern Railway Co., Series "H," 4s, 1946		2,910.45	
5,000	New York Central RR, 3¾s, 1946	4,900.00		
1,000	North American Edison Co., Deb., Series "A," 5s, 1957	1,032.75		
4,000	North American Edison Co., Deb., Series "A," 5s, 1957		4,114.85	
5,000	Northern States Power Co., 1st & Ref. Mort., 3½s, 1967	4,806.25		
2,000	Ohio Edison Co., 1st Mort., 4s, 1965	2,115.00		
3,000	Ohio Edison Co., 1st Mort., 4s, 1965		3,172.50	
5,000	Pennsylvania RR, Gen., 4¼s, Series "E," 1984		5,013.10	
2,000	Port of New York Authority, Interstate Bridge, 4½s, Series "B," 1952	2,042.20		
2,000	Port of New York Authority, Interstate Tunnel, 4¼s, Series "E," 1958	2,065.40		
5,000	Southern Pacific Co., 3¾s, 1946		5,008.65	
5,000	Texas & Pacific Ry. Gen. & Ref., Series "B," 5s, 1977	5,313.40		
2,000	U. S. Treasury, 4s, 1954	1,998.13		
20,000	U. S. Treasury, 3¼s, 1945	19,887.50		
5,000	Virginia Public Service, 5½s, 1946		5,133.65	
$102,000	TOTAL, Bonds	$67,410.43	$34,795.35	$102,205.78
Shares	*Stocks*			
50	American Brake Shoe & Foundry Co., Conv., Pfd.		$ 6,163.60	
50	American Gas & Electric Co., $6.00, Pfd.		5,537.25	
50	Atchison, Topeka & Santa Fe, 5%, Pfd.		4,970.75	
50	Caterpillar Tractor, 5%, Pfd.		5,103.55	
100	Chase Nat'l Bank of New York		4,550.00	
50	Continental Can Co., $4.50, Cum. Pfd.		5,125.00	
50	E. I. du Pont, 6%, Cum., Deb.		6,899.00	
20	J. C. Penney Co.		1,375.30	
50	Johns-Manville Corp., 7%, Cum. Pfd.		6,326.10	
150	Pacific Gas & Electric Co., 6%, Pfd.		4,640.50	
50	Timken Roller Bearing Co.		3,407.25	
50	Union Carbide & Carbon Corp.		3,292.65	
	TOTAL, Stocks		$57,390.95	
	TOTAL, Investments	$67,410.43	$92,186.30	$159,596.73

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These reduced rates will apply exclusively to sufferers from arthritis and all patients admitted will be required to remain three months unless sooner discharged by the Medical Director.

Regular rates will be restored October 15, 1939.

For further information address:

THE DESERT SANATORIUM
Tucson - Arizona

ANNALS OF INTERNAL MEDICINE

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The Annals of Internal Medicine is published by the American College of Physicians. The contents consist of contributions in the field of internal medicine, editorials, book reviews, and a section devoted to the affairs of the College.

Manuscripts. All correspondence relating to the publication of papers and all books and monographs for review should be addressed to the editor. No manuscripts will be accepted without his consideration. Bibliographic references are to conform to the following style:

4. Doe, J. E.: What I know about it, Jr. Am. Med. Assoc., 1931, xcvi, 2006-2008.

Six illustrations per article are allowed without cost to the author. Beyond this number the author must pay the actual cost of illustrations.

Reprints. For each article published, there will be furnished gratis fifty reprints without covers. An order slip for additional reprints, with a table showing cost, will be sent with galley proof to each contributor. If additional reprints over the first fifty are wanted the order slip must be returned to the printer at the time corrected galley proofs are sent to the Editor.

Reviews. The Annals will make an especial feature of the reviews of monographs and books bearing upon the field of internal medicine. Authors and publishers wishing to submit such material should send it to the editor. While obviously impossible to make extended reviews of all material, an acknowledgment of all books and monographs sent will be made in the department of reviews.

Subscription. This periodical is issued monthly, new volumes beginning with the July number each year. Subscriptions may be by the volume or year, but the volume basis is especially recommended. Volumes will consist of approximately 2,000 pages. Subscription price per volume, or per annum, net postpaid: $7.00, United States, Canada, Mexico, Cuba, Canal Zone, Hawaii, Puerto Rico; $7.50, other countries. Prices for back volumes or numbers furnished upon application. Single numbers, current volume, when available, $1.00. Members of the American College of Physicians receive the Annals of Internal Medicine in connection with the payment of annual membership dues, of which seven dollars is for a year's subscription to the publication. Checks should be drawn to the order of W. D. Stroud, M.D., Treasurer, and remitted through the Publication Office or the Executive Secretary's Office.

Business Correspondence. All correspondence relating to business matters, advertising, subscriptions to the Annals, inquiries concerning membership in the American College of Physicians, et cetera, should be addressed to the Publication Office or to the Executive Secretary. Books and reprints presented to the College Library should be addressed to the Executive Secretary.

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